



INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 7 : C07D 277/46, 417/12, A61K 31/426, 31/427, A61P 35/00		A1	(11) International Publication Number: WO 00/26202 (43) International Publication Date: 11 May 2000 (11.05.00)
<p>(21) International Application Number: PCT/EP99/08306</p> <p>(22) International Filing Date: 27 October 1999 (27.10.99)</p> <p>(30) Priority Data: 9823871.0 30 October 1998 (30.10.98) GB</p> <p>(71) Applicant (for all designated States except US): PHARMACIA & UPJOHN S.P.A. [IT/IT]; Via Robert Koch, 1.2, I-20152 Milano (IT).</p> <p>(72) Inventors; and</p> <p>(75) Inventors/Applicants (for US only): PEVARELLO, Paolo [IT/IT]; Piazza San Pietro in Ciel d'Oro, 7/A, I-27100 Pavia (IT). AMICI, Raffaella [IT/IT]; Via N. Rocca, 11, I-29100 Piacenza (IT). TRAQUANDI, Gabriella [IT/IT]; Via F. Cilea, 106, I-20151 Milano (IT). VILLA, Manuela [IT/IT]; Via San Bernardino, 12, I-22040 Lurago d'Erba (IT). VULPETTI, Anna [IT/IT]; Via Volturro Portici/2 80, I-20047 Brugherio (IT). ISACCHI, Antonella [IT/IT]; Via Montecatini, 14, I-20144 Milano (IT).</p>		<p>(81) Designated States: AL, AU, BA, BB, BG, BR, CA, CN, CU, CZ, EE, GE, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, ZA, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).</p> <p>Published With international search report. Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</p>	
<p>(54) Title: 2-AMINO-1,3-thiazole DERIVATIVES, PROCESS FOR THEIR PREPARATION, AND THEIR USE AS ANTITUMOR AGENTS</p> <div style="text-align: center;"> <p style="text-align: center;">(I)</p> </div> <p>(57) Abstract</p> <p>Compounds which are 2-amino-1,3-thiazole derivatives of formula (I) wherein R is a halogen atom, a nitro group, an optionally substituted amino group or it is a group, optionally further substituted, selected from i) straight or branched C₁-C₈ alkyl, C₂-C₆ alkenyl or C₂-C₆ alkynyl; ii) C₃-C₆ cycloalkyl; iii) aryl or arylalkyl with from 1 to 8 carbon atoms within the straight or branched alkyl chain; R₁ is an optionally substituted group selected from: i) straight or branched C₁-C₈ alkyl or C₂-C₆ alkenyl; ii) 3 to 6 membered carbocycle or 5 to 7 membered heterocycle ring; iii) aryl or arylcarbonyl; iv) arylalkyl with from 1 to 8 carbon atoms within the straight or branched alkyl chain; v) arylalkenyl with from 2 to 6 carbon atoms within the straight or branched alkenyl chain; vi) an optionally protected amino acid residue; or a pharmaceutically acceptable salt thereof; are useful for treating cell proliferative disorders associated with an altered cell dependent kinase activity.</p>			

FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AL	Albania	ES	Spain	LS	Lesotho	SI	Slovenia
AM	Armenia	FI	Finland	LT	Lithuania	SK	Slovakia
AT	Austria	FR	France	LU	Luxembourg	SN	Senegal
AU	Australia	GA	Gabon	LV	Latvia	SZ	Swaziland
AZ	Azerbaijan	GB	United Kingdom	MC	Monaco	TD	Chad
BA	Bosnia and Herzegovina	GE	Georgia	MD	Republic of Moldova	TG	Togo
BB	Barbados	GH	Ghana	MG	Madagascar	TJ	Tajikistan
BE	Belgium	GN	Guinea	MK	The former Yugoslav Republic of Macedonia	TM	Turkmenistan
BF	Burkina Faso	GR	Greece	ML	Mali	TR	Turkey
BG	Bulgaria	HU	Hungary	MN	Mongolia	TT	Trinidad and Tobago
BJ	Benin	IE	Ireland	MR	Mauritania	UA	Ukraine
BR	Brazil	IL	Israel	MW	Malawi	UG	Uganda
BY	Belarus	IS	Iceland	MX	Mexico	US	United States of America
CA	Canada	IT	Italy	NE	Niger	UZ	Uzbekistan
CF	Central African Republic	JP	Japan	NL	Netherlands	VN	Viet Nam
CG	Congo	KE	Kenya	NO	Norway	YU	Yugoslavia
CH	Switzerland	KG	Kyrgyzstan	NZ	New Zealand	ZW	Zimbabwe
CI	Côte d'Ivoire	KP	Democratic People's Republic of Korea	PL	Poland		
CM	Cameroon	KR	Republic of Korea	PT	Portugal		
CN	China	KZ	Kazakhstan	RO	Romania		
CU	Cuba	LC	Saint Lucia	RU	Russian Federation		
CZ	Czech Republic	LI	Liechtenstein	SD	Sudan		
DE	Germany	LK	Sri Lanka	SE	Sweden		
DK	Denmark	LR	Liberia	SG	Singapore		
EE	Estonia						

- 1 -

2-AMINO-THIAZOLE DERIVATIVES, PROCESS FOR THEIR PREPARATION, AND THEIR USE AS ANTITUMOR AGENTS.

5

The present invention relates to 2-amino-thiazole derivatives, to a process for their preparation, to pharmaceutical compositions containing them and to their use as therapeutic agents, particularly in the treatment of 10 cancer and cell proliferative disorders.

Several cytotoxic drugs such as, e.g. fluorouracil (5-FU), doxorubicin and camptothecins result to damage DNA or to affect cellular metabolic pathways and thus cause, in many 15 cases, an indirect block of the cell cycle.

Therefore, by producing an irreversible damage to both normal and tumor cells, these agents result in a significant toxicity and side-effects.

In this respect, compounds capable of being highly specific 20 antitumor agents by selectively leading to tumor cell arrest and apoptosis, with comparable efficacy but reduced toxicity than the currently available drugs, are desirable.

It is well known in the art that progression through the 25 cell cycle is governed by a series of checkpoint controls, otherwise referred to as restriction points, which are regulated by a family of enzymes known as the cyclin-dependent kinases (cdk).

In their turn, the cdk's themselves are regulated at many 30 levels such as, for instance, binding to cyclins.

A normal progression through the cell cycle is controlled by the coordinated activation and inactivation of different cyclin/cdk complexes. In G1, both cyclin D/cdk4 and cyclin E/cdk2 are thought to mediate the onset of S-phase. 35 Progression through S-phase requires the activity of cyclin A/cdk2 whereas the activation of cyclin A/cdc2 (cdk1) and cyclin B/cdc2 are required for the onset of metaphases.

For a general reference to cyclins and cyclin-dependent kinases see, for instance, Kevin R. Webster et al. in *Exp. Opin. Invest. Drugs*, 1998, Vol. 7(6), 865-887.

5 Checkpoint controls are defective in tumor cells due, in part, to disregulation of cdk activity. For example, altered expression of cyclin E and cdk's has been observed in tumor cells, and deletion of the cdk inhibitor p27 KIP gene in mice has been shown to result in a higher incidence
10 of cancer.

Increasing evidence supports the idea that the cdk's are rate-limiting enzymes in cell cycle progression and, as such, represent molecular targets for therapeutic intervention. In particular, the direct inhibition of
15 cdk/cyclin kinase activity should be helpful in restricting the unregulated proliferation of a tumor cell.

It has now been found that the 2-amino-1,3-thiazoles of the invention are endowed with cdk/cyclin kinase inhibitory
20 activity and are thus useful in therapy as antitumor agents whilst lacking, in terms of both toxicity and side effects, the aforementioned drawbacks known for currently available antitumor drugs.

More specifically, the compounds of this invention are
25 useful in the treatment of a variety of cancers including, but not limited to: carcinoma such as bladder, breast, colon, kidney, liver, lung, including small cell lung cancer, esophagus, gall-bladder, ovary, pancreas, stomach, cervix, thyroid, prostate, and skin, including squamous
30 cell carcinoma; hematopoietic tumors of lymphoid lineage, including leukemia, acute lymphocytic leukemia, acute lymphoblastic leukemia, B-cell lymphoma, T-cell-lymphoma, Hodgkin's lymphoma, non-Hodgkin's lymphoma, hairy cell lymphoma and Burkett's lymphoma; hematopoietic tumors of
35 myeloid lineage, including acute and chronic myelogenous leukemias, myelodysplastic syndrome and promyelocytic leukemia; tumors of mesenchymal origin, including fibrosarcoma and rhabdomyosarcoma; tumors of the central

and peripheral nervous system, including astrocytoma, neuroblastoma, glioma and schwannomas; other tumors, including melanoma, seminoma, teratocarcinoma, osteosarcoma, xenoderoma pigmentosum, keratoctanthoma, 5 thyroid follicular cancer and Kaposi's sarcoma.

Due to the key role of cdks in the regulation of cellular proliferation, these 2-amino-1,3-thiazole derivatives are also useful in the treatment of a variety of cell 10 proliferative disorders such as, for instance, benign prostate hyperplasia, familial adenomatosis, polyposis, neuro-fibromatosis, psoriasis, vascular smooth cell proliferation associated with atherosclerosis, pulmonary fibrosis, arthritis, glomerulonephritis and post-surgical 15 stenosis and restenosis.

The compounds of the invention can be useful in the treatment of Alzheimer's disease, as suggested by the fact that cdk5 is involved in the phosphorylation of tau protein (J.Biochem., 117, 741-749, 1995).
20 The compounds of this invention, as modulators of apoptosis, could be useful in the treatment of cancer, viral infections, prevention of AIDS development in HIV-infected individuals, autoimmune diseases and neurodegenerative disorder.
25 The compounds of this invention could be useful in inhibiting tumor angiogenesis and metastasis.

The compounds of this invention may also act as inhibitors of other protein kinases, e.g. protein kinase C, her2, 30 raf1, MEK1, MAP kinase, EGF receptor, PDGF receptor, IGF receptor, PI3 kinase, wee1 kinase, Src, Abl and thus be effective in the treatment of diseases associated with other protein kinases.

35 Several 2-amino-1,3-thiazole derivatives are known in the art. Just few examples among them are 2-acetamido-, 2-propionamido- or 2-butyramido-1,3-thiazole derivatives further substituted by halogen atoms in position 5 of the

thiazole ring, which are reported as herbicides in JP 73027467 (Sankyo Co. Ltd.) or US 3,374,082 (The Upjohn Co.); 5-nitro-2-benzamido-1,3-thiazole is reported as pesticide in Ann. Rech. Vet., 22(4), 359-63, 1991; 5-phenyl-2-acetamido-1,3-thiazoles further substituted onto phenyl ring are reported as synthetic intermediates (Chemical Abstracts, 1980, 92:128793); and 5-dimethylaminomethyl- or 5-diethylaminomethyl-2-acetamido-1,3-thiazole, both reported as herbicides in JP 71018564 (Japan Gas Chem Co.).

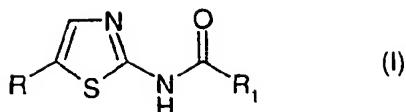
Several other 2-amino-1,3-thiazole derivatives have been reported in the art as useful therapeutic agents.

In particular, 5-methyl-1,3-thiazoles further substituted in position 2 of the thiazole ring by a benzothiazinyl-carbonylamino moiety, or derivatives thereof, have been described as cyclooxygenase inhibitors; see, for instance, C.A. 126(1997):301540.

2-Benzamido-1,3-thiazoles are disclosed in EP-A-261503 (Valeas S.p.A.) as antiallergic agents; 5-Alkyl-2-phenylalkylcarbonylamino-1,3-thiazoles further substituted onto the phenyl ring with an alkenylcarbonyl or alkynylcarbonyl moieties are disclosed in WO 98/04536 (Otsuka Pharmaceutical Co.) as protein kinase C inhibitors. 5-Arylthio-2-acylamino-1,3-thiazole derivatives are disclosed in EP-A-412404 (Fujisawa Pharm. Co.) as antitumor agents.

In addition, among the compounds reported in the art as therapeutic agents, DE 2128941 (Melle-Bezons) discloses 2-aminomethylcarbonylamino-5-chloro-1,3-thiazoles as antiinflammatory, sedative and analgesic agents; the compound 2-diethylaminomethylcarbonylamino-5-chloro-1,3-thiazole being specifically exemplified therein.

Accordingly, the present invention provides the use of a compound which is a 2-amino-1,3-thiazole derivative of formula (I)



wherein

R is a halogen atom, a nitro group, an optionally substituted amino group or it is a group, optionally further substituted, selected from:

- i) straight or branched C₁-C₈ alkyl, C₂-C₆ alkenyl or C₂-C₆ alkynyl;
- ii) C₃-C₆ cycloalkyl;
- iii) aryl or arylalkyl with from 1 to 8 carbon atoms within the straight or branched alkyl chain;

R₁ is an optionally further substituted group selected from:

- i) straight or branched C₁-C₈ alkyl or C₂-C₆ alkenyl;
- ii) 3 to 6 membered carbocycle or 5 to 7 membered heterocycle ring;
- iii) aryl or arylcarbonyl;
- iv) arylalkyl with from 1 to 8 carbon atoms within the straight or branched alkyl chain;
- v) arylalkenyl with from 2 to 6 carbon atoms within the straight or branched alkenyl chain;
- vi) an optionally protected amino acid residue;

or a pharmaceutically acceptable salt thereof; in the manufacture of a medicament for treating cell proliferative disorders associated with an altered cell dependent kinase activity.

According to a preferred embodiment of the invention, the said cell proliferative disorder is selected from the group consisting of cancer, Alzheimer's disease, viral infections, auto-immune diseases or neurodegenerative disorders.

Preferably, the cancer is selected from the group consisting of carcinoma, squamous cell carcinoma, hematopoietic tumors of myeloid or lymphoid lineage, tumors of mesenchymal origin, tumors of the central and peripheral nervous system, melanoma, seminoma, teratocarcinoma,

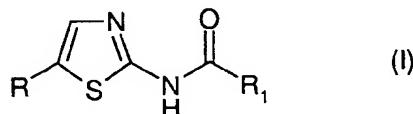
osteosarcoma, | xenoderoma pigmentosum, keratoctanthoma, thyroid follicular cancer and Kaposi's sarcoma.

According to another preferred embodiment of the invention, 5 the cell proliferative disorder is selected from the group consisting of benign prostate hyperplasia, familial adenomatosis polyposis, neuro-fibromatosis, psoriasis, vascular smooth cell proliferation associated with atherosclerosis, pulmonary fibrosis, arthritis 10 glomerulonephritis and post-surgical stenosis and restenosis.

In addition, being useful in the treatment of cell proliferative disorders associated with an altered cell 15 dependent kinase activity, hence cell cycle inhibition or cdk/cyclin dependent inhibition, the compounds of formula (I) of the invention also enable tumor angiogenesis and metastasis inhibition.

20 As above reported, some of the compounds of formula (I) of the invention have been reported in the art as useful therapeutic agents, for instance as antiinflammatory, sedative and analgesic agents.

25 Therefore, it is a further object of the present invention a compound which is a 2-amino-1,3-thiazole derivative of formula (I)



wherein

30 R is a halogen atom, a nitro group, an optionally substituted amino group or it is a group, optionally further substituted, selected from:

- i) straight or branched C₁-C₆ alkyl, C₂-C₆ alkenyl or C₂-C₆ alkynyl;
- 35 ii) C₃-C₆ cycloalkyl;

iii) aryl or arylalkyl with from 1 to 8 carbon atoms within the straight or branched alkyl chain;

R₁ is an optionally further substituted group selected from:

5 i) straight or branched C₁-C₆ alkyl or C₂-C₆ alkenyl;

ii) 3 to 6 membered carbocycle or 5 to 7 membered heterocycle ring;

iii) aryl or arylcarbonyl;

iv) arylalkyl with from 1 to 8 carbon atoms within the straight or branched alkyl chain;

10 v) arylalkenyl with from 2 to 6 carbon atoms within the straight or branched alkenyl chain;

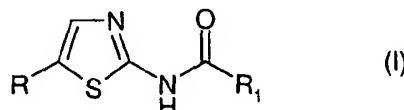
vi) an optionally protected amino acid residue;

or a pharmaceutically acceptable salt thereof; for use as a medicament; provided that each of R and R₁, independently, is not a methyl group and that the compound is not 2-diethylaminomethyl-carbonylamino-5-chloro-1,3-thiazole.

Among the compounds of formula (I) above reported, several

20 derivatives result to be novel.

Therefore, the present invention further provides a compound which is a 2-amino-1,3-thiazole derivative of formula (I)



25 wherein

R is a halogen atom, a nitro group, an optionally substituted amino group or it is a group, optionally further substituted, selected from:

30 i) straight or branched C₁-C₆ alkyl, C₂-C₆ alkenyl or C₂-C₆ alkynyl;

ii) C₃-C₆ cycloalkyl;

iii) aryl or arylalkyl with from 1 to 8 carbon atoms within the straight or branched alkyl chain;

35 R₁ is an optionally further substituted group selected from:

- i) straight or branched C₁-C₈ alkyl or C₂-C₆ alkenyl;
- ii) 3 to 6 membered carbocycle or 5 to 7 membered heterocycle ring;
- iii) aryl or arylcarbonyl;
- 5 iv) arylalkyl with from 1 to 8 carbon atoms within the straight or branched alkyl chain;
- v) arylalkenyl with from 2 to 6 carbon atoms within the straight or branched alkenyl chain;
- vi) an optionally protected amino acid residue;
- 10 or a pharmaceutically acceptable salt thereof;

provided that:

- a) R and R₁, each independently, are not methyl;
- b) when R is bromine or chlorine then, R₁ is not unsubstituted C₂-C₄ alkyl or an optionally substituted 15 aminomethyl;
- c) when R is nitro or phenyl, then R₁ is not unsubstituted phenyl.

20 The compounds of formula (I) may have asymmetric carbon atoms and may therefore exist either as racemic admixtures or as individual optical isomers.

Accordingly, all the possible isomers and their admixtures and of both the metabolites and the pharmaceutically acceptable bio-precursors (otherwise referred to as pro-25 drugs) of the compounds of formula (I), as well as the uses thereof, are also within the scope of the present invention.

30 In the present description, unless otherwise specified, with the term halogen atom we intend a chlorine, bromine, fluorine or iodine atom.

With the term optionally substituted amino group we intend 35 an amino group wherein one or both hydrogen atoms are optionally replaced by other substituents which are the same or different, as set forth below.

With the term straight or branched C₁-C₆ alkyl we intend a group such as, for instance, methyl, ethyl, n.propyl, isopropyl, n.butyl, isobutyl, sec-butyl, tert-butyl, n.pentyl, n.hexyl, n.heptyl, n.octyl and the like.

5

With the term straight or branched C₂-C₆ alkenyl or alkynyl we intend a group such as, for instance, vinyl, allyl, isopropenyl, 1-, 2- or 3-butenyl, isobutylenyl, pentenyl, hexenyl, ethynyl, 1- or 2-propynyl, butynyl, pentynyl, hexynyl and the like.

10

With the term C₃-C₆ cycloalkyl we intend a cyclopropyl, cyclobutyl, cyclopentyl or cyclohexyl group.

15

With the term aryl, either as such or as arylalkyl, arylalkenyl, arylcarbonyl and the like, we intend a mono-, bi- or poly- either carbocyclic as well as heterocyclic hydrocarbon with from 1 to 4 ring moieties, either fused or linked to each other by single bonds, wherein at least one of the carbocyclic or heterocyclic rings is aromatic.

20

Examples of aryl groups are phenyl, indanyl, biphenyl, α- or β-naphthyl, fluorenyl, 9,10-dihydroanthracenyl, pyridyl, pyrazinyl, pyrimidinyl, pyridazinyl, indolyl, imidazolyl, 1,2-methylenedioxophenyl, thiazolyl, isothiazolyl, 25 pyrrolyl, pyrrolyl-phenyl, furyl, phenyl-furyl, benzotetrahydrofuran, oxazolyl, isoxazolyl, pyrazolyl, chromenyl, thienyl, benzothienyl, isoindolinyl, benzoimidazolyl, tetrazolyl, tetrazolylphenyl, pyrrolidinyl-tetrazolyl, isoindolinyl-phenyl, quinolinyl, 30 isoquinolinyl, 2,6-diphenyl-pyridyl, quinoxalinyl, pyrazinyl, phenyl-quinolyl, benzofurazanyl, 1,2,3-triazole, 1-phenyl-1,2,3-triazole, and the like.

25

With the term 3 to 6 membered carbocycle, hence encompassing but not limited to C₃-C₆ cycloalkyl groups, we also intend an unsaturated carbocyclic hydrocarbon such as, for instance, cyclopentylene or cyclohexylene.

With the term 5 to 7 membered heterocycle, hence encompassing aromatic heterocycles also referred to as aryl groups, we further intend a saturated or partially unsaturated 5 to 7 membered carbocycle wherein one or more 5 carbon atoms are replaced by heteroatoms such as nitrogen, oxygen and sulphur.

Examples of 5 to 7 membered heterocycles, optionally benzocondensed or further substituted, are 1,3-dioxolane, 10 pyran, pyrrolidine, pyrroline, imidazolidine, pyrazolidine, pyrazoline, piperidine, piperazine, N-alkyl-piperazine, morpholine, tetrahydrofuran and the like.

With the term amino acid residue we intend the residue of a natural α -amino acid of formula HOOC-R₁, wherein R₁ is 15 bonded to the thiazole-NH-C(=O)- moiety and is represented by a -CH(Z)NHY group wherein Z is the characterising portion of the amino acid and Y is hydrogen or a suitable amino protecting group such as, for instance, tert-butoxycarbonyl or benzyloxycarbonyl.

20 Examples of α -amino acids are alanine, isoleucine, glycine, lysine, arginine, cystine, histidine, leucine, proline and the like.

According to the above indicated substituent meanings, any 25 of the above R and R₁ groups may be optionally substituted in any of the free positions by one or more groups, for instance 1 to 6 groups, selected from: halogen, nitro, oxo groups (=O), carboxy, cyano, alkyl, perfluorinated alkyl, alkenyl, alkynyl, cycloalkyl, aryl, heterocycyl; amino 30 groups and derivatives thereof such as, for instance, alkylamino, alkoxycarbonylalkylamino, dialkylamino, arylamino, diarylamino or arylureido; carbonylamino groups and derivatives thereof such as, for instance, hydrogenocarbonylamino (HCONH-), alkylcarbonylamino, 35 alkenylcarbonylamino, arylcarbonylamino, alkoxycarbonylamino; oxygen-substituted oximes such as, for instance, alkoxycarbonylalkoxyimino or alkoxyimino; hydroxy

groups and derivatives thereof such as, for instance, alkoxy, aryloxy, alkylcarbonyloxy, arylcarbonyloxy, cycloalkenyloxy; carbonyl groups and derivatives thereof such as, for instance, alkylcarbonyl, arylcarbonyl, 5 alkoxy carbonyl, aryloxy carbonyl, cycloalkyloxycarbonyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl; sulfurated derivatives such as, for instance, alkylthio, arylthio, alkylsulphonyl, arylsulphonyl, alkylsulphanyl, arylsulphanyl, arylsulphonyloxy, aminosulfonyl, 10 alkylaminosulphonyl or dialkylaminosulphonyl. In their turn, whenever appropriate, each of the above possible substituents on R and R₁ may be further substituted by one or more of the aforementioned groups.

Examples of compounds of formula (I) wherein R and R₁ groups 15 are substituted by one or more of the aforementioned substituents which, in their turn, are optionally further substituted as set forth above, are given below.

Pharmaceutically acceptable salts of the compounds of 20 formula (I) are the acid addition salts with inorganic or organic, e.g. nitric, hydrochloric, hydrobromic, sulphuric, perchloric, phosphoric, acetic, trifluoroacetic, propionic, glycolic, lactic, oxalic, malonic, malic, maleic, tartaric, citric, benzoic, cinnamic, mandelic, methanesulphonic, 25 isethionic and salicylic acid, as well as the salts with inorganic or organic bases, e.g. alkali or alkaline-earth metals, especially sodium, potassium, calcium or magnesium hydroxides, carbonates or bicarbonates, acyclic or cyclic amines, preferably methylamine, ethylamine, diethylamine, 30 triethylamine or piperidine.

The compounds of formula (I) may have asymmetric carbon atoms and may therefore exist either as racemic admixtures or as individual optical isomers.

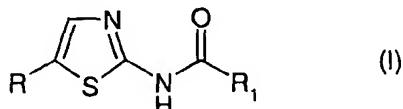
35 Accordingly, the use as an antitumor agent of all the possible isomers and their admixtures and of both the metabolites and the pharmaceutically acceptable bio-precursors (otherwise referred to as pro-drugs) of the

compounds of formula (I) are also within the scope of the present invention.

Preferred compounds of formula (I), according to the 5 present invention, are 2-amino-1,3-thiazole derivatives wherein R is a halogen atom or an optionally substituted group selected from a straight or branched C₁-C₄ alkyl, C₃-C₆ cycloalkyl, aryl or an arylalkyl with from 1 to 4 carbon atoms within the alkyl chain; R₁ is an optionally 10 substituted group selected from straight or branched C₁-C₄ alkyl or alkenyl, aryl or arylalkyl with from 1 to 4 carbon atoms within the alkyl chain or it is an optionally protected amino acid residue.

15 Still more preferred compounds, within this class, are the derivatives of formula (I) wherein R is a bromine or chlorine atom or is an optionally substituted group selected from straight or branched C₁-C₄ alkyl, cyclopropyl, aryl or arylalkyl with from 1 to 2 carbon atoms within the 20 alkyl chain; R₁ is an optionally substituted group selected from straight or branched C₁-C₄ alkyl or alkenyl, aryl or arylalkyl with from 1 to 4 carbon atoms within the alkyl chain or it is an optionally protected amino acid residue.

25 Another class of preferred compounds of the invention are the compounds of formula (I)



wherein

R is a halogen atom or is selected from nitro, amino, 30 alkylamino, hydroxyalkylamino, arylamino, C₃-C₆ cycloalkyl and straight or branched C₁-C₆ alkyl which is unsubstituted or substituted by hydroxy, alkylthio, alkoxy, amino, alkylamino, alkoxy carbonylamino, alkoxy carbonylalkylamino, alkylcarbonyl, alkylsulfonyl, 35 alkoxy carbonyl, carboxy or aryl which is unsubstituted

or substituted by one or more hydroxy, halogen, nitro, alkoxy, aryloxy, alkylthio, arylthio, amino, alkylamino, dialkylamino, N-alkyl-piperazinyl, 4-morpholinyl, arylamino, cyano, alkyl, phenyl, 5 aminosulfonyl, aminocarbonyl, alkylcarbonyl, arylcarbonyl, alkoxycarbonyl or carboxy groups, or R is an aryl group which is unsubstituted or substituted by one or more hydroxy, halogen, nitro, alkoxy, aryloxy, alkylthio, arylthio, amino, alkylamino, dialkylamino, 10 N-alkyl-piperazinyl, 4-morpholinyl, arylamino, cyano, alkyl, phenyl, aminosulphonyl, aminocarbonyl, alkylcarbonyl, arylcarbonyl, alkoxycarbonyl or carboxy groups;

15 R_1 is a straight or branched C_1-C_6 alkyl group or an aryl group, each being unsubstituted or substituted as defined above for R;

or a pharmaceutically acceptable salt thereof;

provided that:

- a) R and R_1 , each independently, are not methyl;
- 20 b) when R is bromine or chlorine then, R_1 is not unsubstituted C_2-C_4 alkyl or an optionally substituted aminomethyl;
- c) when R is nitro or phenyl, then R_1 is not unsubstituted phenyl.

25

Examples of preferred compounds of the invention, whenever appropriate in the form of pharmaceutically acceptable salts, e.g. hydrobromide or hydrochloride salt, are the following:

- 30 1. ethyl 3-[(5-bromo-1,3-thiazol-2-yl)amino]-3-oxopropanoate;
- 2. N-(5-bromo-1,3-thiazol-2-yl)-2-phenyl-acetamide;
- 3. N-(5-bromo-1,3-thiazol-2-yl)-benzamide;
- 4. Ethyl 4-[(5-bromo-1,3-thiazol-2-yl)amino]-4-oxobutanoate;
- 35 5. N-(5-Bromo-thiazol-2-yl)-3-hydroxy-propionamide;
- 6. N-(5-Bromo-1,3-thiazol-2-yl)-4-hydroxybutanamide;

7. N-(5-Bromo-thiazol-2-yl)-2-ethoxy-acetamide;
8. 2-N-[2-(3-pyridyl)-acetyl-amino]-5-bromo-thiazole;
9. 2-N-[2-(3-pyridyl)-acetyl-amino]-5-isopropyl-thiazole;
10. N-(5-bromo-1,3-thiazol-2-yl)-2-(3-hydroxyphenyl)acetamide;
11. N-(5-isopropyl-1,3-thiazol-2-yl)-2-(3-hydroxyphenyl)acetamide
12. N-(5-bromo-1,3-thiazol-2-yl)-2-(3-methoxyphenyl)acetamide;
13. N-(5-isopropyl-1,3-thiazol-2-yl)-2-(3-methoxyphenyl)acetamide;
14. N-(5-bromo-1,3-thiazol-2-yl)-2-(3-chlorophenyl)acetamide;
15. N-(5-isopropyl-1,3-thiazol-2-yl)-2-(3-chlorophenyl)acetamide;
16. N-(5-bromo-1,3-thiazol-2-yl)-2-(4-hydroxyphenyl)acetamide;
17. N-(5-isopropyl-1,3-thiazol-2-yl)-2-(4-hydroxyphenyl)acetamide;
18. N-(5-bromo-1,3-thiazol-2-yl)-2-(3,4-dihydroxyphenyl)acetamide;
19. N-(5-isopropyl-1,3-thiazol-2-yl)-2-(3,4-dihydroxyphenyl)acetamide;
20. N-(5-bromo-1,3-thiazol-2-yl)-2-(4-hydroxy-3-methoxyphenyl)acetamide;
21. N-(5-isopropyl-1,3-thiazol-2-yl)-2-(4-hydroxy-3-methoxyphenyl)acetamide;
22. N-(5-bromo-1,3-thiazol-2-yl)-2-(4-methoxyphenyl)acetamide;
23. N-(5-isopropyl-1,3-thiazol-2-yl)-2-(4-methoxyphenyl)acetamide;
24. N-(5-isopropyl-1,3-thiazol-2-yl)-2-(4-chlorophenyl)acetamide;
25. N-(5-isopropyl-1,3-thiazol-2-yl)-2-phenyl-acetamide;
26. N-(5-bromo-thiazol-2-yl)-4-sulfamoyl-benzamide;
27. N-(5-isopropyl-thiazol-2-yl)-4-sulfamoyl-benzamide;
28. 4-amino-N-(5-bromo-1,3-thiazol-2-yl)butanamide;

29. 3-amino-N-(5-bromo-1,3-thiazol-2-yl)propionamide;
30. N-(5-isopropyl-1,3-thiazol-2-yl)-butanamide;
31. N-(5-bromo-1,3-thiazol-2-yl)-butanamide;
32. N-(5-chloro-1,3-thiazol-2-yl)-butanamide;
5 33. N-(5-phenyl-1,3-thiazol-2-yl)-butanamide;
34. N-(5-nitro-1,3-thiazol-2-yl)-butanamide;
35. N-(5-methyl-1,3-thiazol-2-yl)-butanamide;
36. N-(5-benzyl-1,3-thiazol-2-yl)-butanamide;
37. N-(5-isobutyl-1,3-thiazol-2-yl)-butanamide;
10 38. N-(5-cyclopropyl-1,3-thiazol-2-yl)-butanamide;
39. N-{5-[2-(methylsulfonyl)ethyl]-1,3-thiazol-2-yl}-
butanamide;
40. N-[5-(2-methylthioethyl)-1,3-thiazol-2-yl]-butanamide;
41. N-{5-[2-(methoxycarbonyl)ethyl]-1,3-thiazol-2-yl}-
15 butanamide;
42. N-[5-(3-methoxy-propyl)-1,3-thiazol-2-yl]-butanamide;
43. N-[5-(2-ethoxy-ethyl)-1,3-thiazol-2-yl]-butanamide;
44. N-[5-(indol-3-yl-methyl)-1,3-thiazol-2-yl]-butanamide;
45. N-[5-(3-oxo-butyl)-1,3-thiazol-2-yl]-butanamide;
20 46. 2-[3-(3-chloropropoxy)phenyl]-N-(5-isopropyl-1,3-
thiazol-2-yl)acetamide
47. 2-[3-(2-chloroethoxy)phenyl]-N-(5-isopropyl-1,3-
thiazol-2-yl)acetamide
48. 2-(4-aminophenyl)-N-(5-isopropyl-1,3-thiazol-2-
25 yl)acetamide
49. 4-amino-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide
50. 2-(2-amino-1,3-thiazol-4-yl)-N-(5-isopropyl-1,3-
thiazol-2-yl)acetamide
51. N-(5-isopropyl-1,3-thiazol-2-yl)-2-{3-[3-(4-
30 morpholinyl)propoxy]phenyl}acetamide
52. N-(5-isopropyl-1,3-thiazol-2-yl)-2-{3-[2-(4-
morpholinyl)ethoxy]phenyl}acetamide
53. N-(5-isopropyl-1,3-thiazol-2-yl)-2-{3-[3-(1-
pirrolidinyl)propoxy]phenyl}acetamide
35 54. N-(5-isopropyl-1,3-thiazol-2-yl)-2-{3-[3-(4-methyl-1-
piperazinyl)propoxy]phenyl}acetamide

55. 2-{3-[2-(dimethylamino)ethoxy]phenyl}-N-(5-isopropyl-1,3-thiazol-2-yl)acetamide;
56. 2-{3-[3-(dimethylamino)propoxy]phenyl}-N-(5-isopropyl-1,3-thiazol-2-yl)acetamide
- 5 57. 2-[4-(dimethylamino)phenyl]-N-(5-isobutyl-1,3-thiazol-2-yl)acetamide
58. 2-(1,3-benzodioxol-5-yl)-N-(5-isobutyl-1,3-thiazol-2-yl)acetamide
59. N-(5-benzyl-1,3-thiazol-2-yl)-2-[4-(dimethylamino)phenyl]acetamide
- 10 60. N-(5-isopropyl-1,3-thiazol-2-yl)-2-[3-(2-methoxyethoxy)-phenyl]acetamide
61. 3-chloro-N-(5-isopropyl-1,3-thiazol-2-yl)-4-(4-methyl-1-piperazinyl)benzamide
- 15 62. N-(5-isobutyl-1,3-thiazol-2-yl)-2-(3-pyridinyl)acetamide
63. N-(5-benzyl-1,3-thiazol-2-yl)-2-(3-pyridinyl)acetamide
64. 2-[N-[2'-N'-(ethoxycarbonyl-methyl)-amino]-acetyl]-amino-5-bromo-thiazole
- 20 65. 2-anilino-N-(5-isopropyl-1,3-thiazol-2-yl)acetamide
66. (R)-N-(5-isopropyl-1,3-thiazol-2-yl)-2-phenylpropanamide
67. (S)-N-(5-isopropyl-1,3-thiazol-2-yl)-2-phenylpropanamide
- 25 68. N-(5-isopropyl-1,3-thiazol-2-yl)benzamide
69. 2,5-dichloro-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide
70. 3,5-dichloro-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide
71. 3,4-dichloro-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide
- 30 72. 2,4-dichloro-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide
73. 2,3-dichloro-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide
74. 3-iodio-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide
75. 2-iodio-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide
76. 4-iodio-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide
- 35 77. 3-bromo-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide
78. 4-chloro-2-fluoro-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide

WO 00/26202

-17-

79. 5-bromo-2-chloro-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide

80. 3-chloro-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide

81. 2-chloro-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide

82. 4-fluoro-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide

83. 3-fluoro-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide

84. 2-fluoro-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide

85. 4-fluoro-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide

86. 2,4-difluoro-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide

87. 3,4-difluoro-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide

88. 2,3,4,5,6-pentafluoro-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide

89. N-(5-isopropyl-1,3-thiazol-2-yl)-4-methyl-3-nitrobenzamide

90. N-(5-isopropyl-1,3-thiazol-2-yl)-5-methyl-2-nitrobenzamide

91. N-(5-isopropyl-1,3-thiazol-2-yl)-3-methyl-2-nitrobenzamide

92. N-(5-isopropyl-1,3-thiazol-2-yl)-3,5-dimethyl-4-nitrobenzamide

93. N-(5-isopropyl-1,3-thiazol-2-yl)-4-methoxy-2-nitrobenzamide

94. N-(5-isopropyl-1,3-thiazol-2-yl)-3-methoxy-2-nitrobenzamide

95. N-(5-isopropyl-1,3-thiazol-2-yl)-4-methoxy-3-nitrobenzamide

96. N-(5-isopropyl-1,3-thiazol-2-yl)-3-methoxy-4-nitrobenzamide

97. N-(5-isopropyl-1,3-thiazol-2-yl)-3,5-dinitrobenzamide

98. 5-[(5-isopropyl-1,3-thiazol-2-yl)-3-nitrobenzamido]octanoate

99. N-(5-isopropyl-1,3-thiazol-2-yl)-2-nitrobenzamide

100. N-(5-isopropyl-1,3-thiazol-2-yl)-4-nitrobenzamide

101. N-(5-isopropyl-1,3-thiazol-2-yl)-4-(methylsulfonyl)-3-nitrobenzamide

102. N-(5-isopropyl-1,3-thiazol-2-yl)-4-(methylsulfonyl)-3-nitrobenzamide

103. 4-chloro-N-(5-isopropyl-1,3-thiazol-2-yl)-3-nitrobenzamide

104. 6-chloro-N-(5-isopropyl-1,3-thiazol-2-yl)-3-nitrobenzamide
105. 4-chloro-N-(5-isopropyl-1,3-thiazol-2-yl)-2-nitrobenzamide
- 5 106. 2-chloro-N-(5-isopropyl-1,3-thiazol-2-yl)-4-nitrobenzamide
107. 5-chloro-N-(5-isopropyl-1,3-thiazol-2-yl)-2-nitrobenzamide
108. 2-bromo-N-(5-isopropyl-1,3-thiazol-2-yl)-5-nitrobenzamide
- 10 109. 4-fluoro-N-(5-isopropyl-1,3-thiazol-2-yl)-3-nitrobenzamide
110. 4-fluoro-N-(5-isopropyl-1,3-thiazol-2-yl)-2-nitrobenzamide
- 15 111. N-(5-isopropyl-1,3-thiazol-2-yl)-2-nitro-4-(trifluoromethyl)benzamide
112. N-(5-isopropyl-1,3-thiazol-2-yl)-3,5-bis(trifluoromethyl)benzamide
113. N-(5-isopropyl-1,3-thiazol-2-yl)-2,6-bis(trifluoromethyl)benzamide
- 20 114. N-(5-isopropyl-1,3-thiazol-2-yl)-2-(trifluoromethyl)benzamide
115. N-(5-isopropyl-1,3-thiazol-2-yl)-3-(trifluoromethyl)benzamide
- 25 116. 3-fluoro-N-(5-isopropyl-1,3-thiazol-2-yl)-4-(trifluoromethyl)benzamide
117. 2-fluoro-N-(5-isopropyl-1,3-thiazol-2-yl)-3-(trifluoromethyl)benzamide
118. 5-fluoro-N-(5-isopropyl-1,3-thiazol-2-yl)-3-(trifluoromethyl)benzamide
- 30 119. 2-fluoro-N-(5-isopropyl-1,3-thiazol-2-yl)-4-(trifluoromethyl)benzamide
120. 4-fluoro-N-(5-isopropyl-1,3-thiazol-2-yl)-3-(trifluoromethyl)benzamide
- 35 121. methyl 4-[(5-isopropyl-1,3-thiazol-2-yl)amino]carbonylbenzoate
122. methyl 2-[(5-isopropyl-1,3-thiazol-2-yl)amino]carbonylbenzoate

123. 4-cyano-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide
124. 3-cyano-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide
125. N-(5-isopropyl-1,3-thiazol-2-yl)-3-methylbenzamide
126. N-(5-isopropyl-1,3-thiazol-2-yl)-2-methylbenzamide
- 5 127. N-(5-isopropyl-1,3-thiazol-2-yl)-4-methylbenzamide
128. N-(5-isopropyl-1,3-thiazol-2-yl)-4-vinylbenzamide
129. N-(5-isopropyl-1,3-thiazol-2-yl)-4-(2-phenylethynyl)benzamide
- 10 130. N-(5-isopropyl-1,3-thiazol-2-yl)-3-methoxy-4-methylbenzamide
131. 2-benzyl-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide
132. N-(5-isopropyl-1,3-thiazol-2-yl)-2-phenethylbenzamide
133. N-(5-isopropyl-1,3-thiazol-2-yl)-2-phenylbenzamide
134. N-(5-isopropyl-1,3-thiazol-2-yl)-4-phenylbenzamide
- 15 135. 4-(tert-butyl)-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide
136. N-(5-isopropyl-1,3-thiazol-2-yl)-4-isopropylbenzamide
137. N-(5-isopropyl-1,3-thiazol-2-yl)-4-pentylbenzamide
138. 3-fluoro-N-(5-isopropyl-1,3-thiazol-2-yl)-4-methylbenzamide
- 20 139. N-(5-isopropyl-1,3-thiazol-2-yl)-3,4-dimethylbenzamide
140. N-(5-isopropyl-1,3-thiazol-2-yl)-3,5-dimethylbenzamide
141. 4-acetyl-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide
142. N-(5-isopropyl-1,3-thiazol-2-yl)-4-(methylsulfonyl)benzamide
- 25 143. 5-(aminosulfonyl)-2,4-dichloro-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide
144. 5-(aminosulfonyl)-4-chloro-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide
- 30 145. 3-fluoro-N-(5-isopropyl-1,3-thiazol-2-yl)-4-methoxybenzamide
146. 3-chloro-N-(5-isopropyl-1,3-thiazol-2-yl)-4-methoxybenzamide
147. 5-chloro-N-(5-isopropyl-1,3-thiazol-2-yl)-2-methoxybenzamide
- 35 148. N-(5-isopropyl-1,3-thiazol-2-yl)-4-methoxybenzamide
149. N-(5-isopropyl-1,3-thiazol-2-yl)-3-methoxybenzamide
150. N-(5-isopropyl-1,3-thiazol-2-yl)-2-methoxybenzamide

WO 00/26202

- 20 -

151. N-(5-isopropyl-1,3-thiazol-2-yl)-3,4-dimethoxybenzamide

152. N-(5-isopropyl-1,3-thiazol-2-yl)-3,5-dimethoxybenzamide

5 153. N-(5-isopropyl-1,3-thiazol-2-yl)-2,4-dimethoxybenzamide

154. N-(5-isopropyl-1,3-thiazol-2-yl)-2,3-dimethoxybenzamide

10 155. N-(5-isopropyl-1,3-thiazol-2-yl)-3-phenoxybenzamide

156. N-(5-isopropyl-1,3-thiazol-2-yl)-2-phenoxybenzamide

157. N-(5-isopropyl-1,3-thiazol-2-yl)-4-phenoxybenzamide

158. 2-ethoxy-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide

159. 4-ethoxy-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide

160. N-(5-isopropyl-1,3-thiazol-2-yl)benzamide

15 161. 3,4,5-trimethoxybenzamide

162. 3,4,5-triethoxy-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide

163. N-(5-isopropyl-1,3-thiazol-2-yl)-3-methoxy-4-(methoxymethoxy)benzamide

20 164. 4-butoxy-N-(5-isopropyl-1,3-thiazol-2-yl)-4-propoxybenzamide

165. N-(5-isopropoxy-N-(5-isopropyl-1,3-thiazol-2-yl)-1,3-benzodioxole-5-

166. 4-isopropoxy-N-(5-isopropyl-1,3-thiazol-2-yl)-1,3-benzodioxole-5-

25 167. N-(5-isopropyl-1,3-thiazol-2-yl)-4-(benzyloxy)-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide

168. 4-(benzyloxy)-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide

169. 4-(2-cyclohexen-1-yloxy)-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide

30 170. N-(5-isopropyl-1,3-thiazol-2-yl)-4-(trifluoromethoxy)benzamide

171. 4-(difluoromethoxy)-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide

35 172. N-(5-(methylsulfanyl)benzyl)-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide

173. 2-[(4-chlorophenyl)sulfinyl]-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide

174. N-(5-isopropyl-1,3-thiazol-2-yl)-2-[(4-nitrophenyl)sulfinyl]benzamide
175. N-(5-isopropyl-1,3-thiazol-2-yl)-4-[(4-methylphenyl)sulfonyl]-3-nitrobenzamide
- 5 176. N-(5-isopropyl-1,3-thiazol-2-yl)-3-[(trifluoromethyl)sulfanyl]benzamide
177. N-(5-isopropyl-1,3-thiazol-2-yl)-2-methoxy-4-(methylsulfanyl)benzamide
- 10 178. 2-[(2-cyanophenyl)sulfanyl]-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide
179. N~1~, N~1~-diethyl-3,6-difluoro-N~2~- (5-isopropyl-1,3-thiazol-2-yl)phthalamide
180. 4-formyl-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide
181. 2-formyl-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide
- 15 182. 4-{{(2,5-dimethoxyanilino)carbonyl}amino}-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide
183. 4-(hydroxymethyl)-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide
184. 4-{{(5-isopropyl-1,3-thiazol-2-yl)amino}carbonyl}-2-nitrobenzyl acetate
- 20 185. 4-{{(5-isopropyl-1,3-thiazol-2-yl)amino}carbonyl}-2-nitrobenzyl 4-(acetylamino)-3-iodobenzoate
186. 4-(acetylamino)-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide
- 25 187. N-(5-isopropyl-1,3-thiazol-2-yl)-4-[(2-phenylacetyl)amino]benzamide
188. 4-(acetylamino)-3-iodo-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide
189. 4-amino-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide
- 30 190. 4-(dimethylamino)-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide
191. 3-(dimethylamino)-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide
192. 2-(methylamino)-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide
- 35 193. N-(5-isopropyl-1,3-thiazol-2-yl)-2-[3-(trifluoromethyl)anilino]benzamide

194. 3-{{(5-bromo-1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl)methyl}amino}-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide

195. N-(5-isopropyl-1,3-thiazol-2-yl)-4-(1H-pyrrol-1-yl)benzamide

196. 2,6-dichloro-N-(5-isopropyl-1,3-thiazol-2-yl)isonicotinamide

197. 2-(4-bromophenyl)-6-(4-iodophenyl)-N-(5-isopropyl-1,3-thiazol-2-yl)isonicotinamide

198. N-(5-isopropyl-1,3-thiazol-2-yl)-2-[3-(trifluoromethyl)anilino]nicotinamide

199. 2,6-dichloro-N-(5-isopropyl-1,3-thiazol-2-yl)nicotinamide

200. 5,6-dichloro-N-(5-isopropyl-1,3-thiazol-2-yl)nicotinamide

201. 2-chloro-N-(5-isopropyl-1,3-thiazol-2-yl)-6-methylnicotinamide

202. 2,6-dichloro-5-fluoro-N-(5-isopropyl-1,3-thiazol-2-yl)nicotinamide

203. N-(5-isopropyl-1,3-thiazol-2-yl)-2-phenoxylicotinamide

204. N-(5-isopropyl-1,3-thiazol-2-yl)-6-(2,2,2-trifluoroethoxy)nicotinamide

205. N-(5-isopropyl-1,3-thiazol-2-yl)-2,6-dimethoxynicotinamide

206. N-(5-isopropyl-1,3-thiazol-2-yl)-2-quinoxalinecarboxamide

207. N-(5-isopropyl-1,3-thiazol-2-yl)-5-methyl-2-pyrazinecarboxamide

208. N-(5-isopropyl-1,3-thiazol-2-yl)-8-quinolinecarboxamide

209. N-(5-isopropyl-1,3-thiazol-2-yl)-2-phenyl-4-quinolinecarboxamide

210. N-(5-isopropyl-1,3-thiazol-2-yl)-5-methyl-1-phenyl-1H-pyrazole-4-carboxamide

211. N-(5-isopropyl-1,3-thiazol-2-yl)-5-methyl-1H-pyrazole-3-carboxamide

212. N-(5-isopropyl-1,3-thiazol-2-yl)-1H-pyrazole-4-carboxamide

213. N-(5-isopropyl-1,3-thiazol-2-yl)-5-methyl-2-phenyl-2H-1,2,3-triazole-4-carboxamide

214. 2-[(2,1,3-benzoxadiazol-5-yloxy)methyl]-N-(5-isopropyl-1,3-thiazol-2-yl)-4-methyl-1,3-thiazole-5-carboxamide

5 215. N-(5-isopropyl-1,3-thiazol-2-yl)-9H-fluorene-1-carboxamide

216. N-(5-isopropyl-1,3-thiazol-2-yl)-7-methoxy-1-benzofuran-2-carboxamide

10 217. N-(5-isopropyl-1,3-thiazol-2-yl)-1-[(4-methylphenyl)sulfonyl]-1H-pyrrole-3-carboxamide

218. 2-ethoxy-N-(5-isopropyl-1,3-thiazol-2-yl)-1-naphthamide

219. 4-fluoro-N-(5-isopropyl-1,3-thiazol-2-yl)-1-naphthamide

15 220. N-(5-isopropyl-1,3-thiazol-2-yl)-2-naphthamide

221. N-(5-isopropyl-1,3-thiazol-2-yl)-9,10-dioxo-9,10-dihydro-2-anthracenecarboxamide

222. N-(5-isopropyl-1,3-thiazol-2-yl)-9-oxo-9H-fluorene-4-carboxamide

20 223. N-(5-isopropyl-1,3-thiazol-2-yl)-9-oxo-9H-fluorene-1-carboxamide

224. N-(5-isopropyl-1,3-thiazol-2-yl)-8-oxo-5,6,7,8-tetrahydro-2-naphthalenecarboxamide

25 225. N-(5-isopropyl-1,3-thiazol-2-yl)-1,3-dioxo-1,3-dihydro-2-benzofuran-5-carboxamide

226. N-(5-isopropyl-1,3-thiazol-2-yl)-1H-indole-5-carboxamide

227. N-(5-isopropyl-1,3-thiazol-2-yl)-1H-indole-4-carboxamide

30 228. N-(5-isopropyl-1,3-thiazol-2-yl)-1-methyl-2-phenyl-1H-indole-5-carboxamide

229. 2-butyl-N-(5-isopropyl-1,3-thiazol-2-yl)-1-methyl-1H-indole-5-carboxamide

35 230. N-(5-isopropyl-1,3-thiazol-2-yl)-1H-indole-6-carboxamide

231. N-(5-isopropyl-1,3-thiazol-2-yl)-5-methoxy-1H-indole-2-carboxamide

232. 1-allyl-2-butyl-N-(5-isopropyl-1,3-thiazol-2-yl)-1H-indole-5-carboxamide

233. N-(5-isopropyl-1,3-thiazol-2-yl)-1-methyl-1H-indole-2-carboxamide

5 234. 1-benzyl-N-(5-isopropyl-1,3-thiazol-2-yl)-2-phenyl-1H-indole-5-carboxamide

235. N-(5-isopropyl-1,3-thiazol-2-yl)-1H-1,2,3-benzotriazole-5-carboxamide

236. N-(5-isopropyl-1,3-thiazol-2-yl)-3,5-dimethyl-4-isoxazolecarboxamide

10 237. N-(5-isopropyl-1,3-thiazol-2-yl)-3-thiophenecarboxamide

238. N-(5-isopropyl-1,3-thiazol-2-yl)-3-methyl-2-thiophenecarboxamide

15 239. N-(5-isopropyl-1,3-thiazol-2-yl)-5-methyl-2-thiophenecarboxamide

240. 5-bromo-N-(5-isopropyl-1,3-thiazol-2-yl)-2-thiophenecarboxamide

241. N-(5-isopropyl-1,3-thiazol-2-yl)-3-[(2,3,3-trichloroacryloyl)amino]-2-thiophenecarboxamide

20 242. 5-bromo-N-(5-isopropyl-1,3-thiazol-2-yl)-2-furamide

243. N-(5-isopropyl-1,3-thiazol-2-yl)-2-furamide

244. N-(5-isopropyl-1,3-thiazol-2-yl)-5-(4-nitrophenyl)-2-furamide

25 245. N-(5-isopropyl-1,3-thiazol-2-yl)-5-(2-nitrophenyl)-2-furamide

246. 5-(4-chlorophenyl)-N-(5-isopropyl-1,3-thiazol-2-yl)-2-furamide

247. N-(5-isopropyl-1,3-thiazol-2-yl)-5-[3-(trifluoromethyl)phenyl]-2-furamide

30 248. 5-(4-chloro-2-nitrophenyl)-N-(5-isopropyl-1,3-thiazol-2-yl)-2-furamide

249. N-(5-isopropyl-1,3-thiazol-2-yl)-5-(4-methyl-2-nitrophenyl)-2-furamide

35 250. 5-[2-chloro-5-(trifluoromethyl)phenyl]-N-(5-isopropyl-1,3-thiazol-2-yl)-2-furamide

251. tert-butyl (1R)-2-[(5-isopropyl-1,3-thiazol-2-yl)amino]-2-oxo-1-phenylethylcarbamate

252. (1R)-2-[(5-isopropyl-1,3-thiazol-2-yl)amino]-2-oxo-1-phenylethyl acetate

253. (1S)-2-[(5-isopropyl-1,3-thiazol-2-yl)amino]-2-oxo-1-phenylethyl acetate

5 254. (R,S)-2-fluoro-N-(5-isopropyl-1,3-thiazol-2-yl)-2-phenylacetamide

255. (R)-2-fluoro-N-(5-isopropyl-1,3-thiazol-2-yl)-2-phenylacetamide

10 256. (S)-2-fluoro-N-(5-isopropyl-1,3-thiazol-2-yl)-2-phenylacetamide

257. 2-(acetylamino)-N-(5-isopropyl-1,3-thiazol-2-yl)-2-phenylacetamide

258. (R,S)-2-(methoxy)-N-(5-isopropyl-1,3-thiazol-2-yl)-2-phenylacetamide

15 259. (R)-2-(methoxy)-N-(5-isopropyl-1,3-thiazol-2-yl)-2-phenylacetamide

260. (S)-2-(methoxy)-N-(5-isopropyl-1,3-thiazol-2-yl)-2-phenylacetamide

20 261. 3,3,3-trifluoro-N-(5-isopropyl-1,3-thiazol-2-yl)-2-methoxy-2-phenylpropanamide

262. N-(5-isopropyl-1,3-thiazol-2-yl)-2-(1-naphthyl)acetamide

263. N-(5-isopropyl-1,3-thiazol-2-yl)-2-(2-naphthyl)acetamide

25 264. 2-(1H-indol-3-yl)-N-(5-isopropyl-1,3-thiazol-2-yl)acetamide

265. 2-(1,3-benzodioxol-4-yl)-N-(5-isopropyl-1,3-thiazol-2-yl)acetamide

266. 2-(2,4-dinitrophenyl)-N-(5-isopropyl-1,3-thiazol-2-yl)acetamide

30 267. N-(5-isopropyl-1,3-thiazol-2-yl)-2-(2-methyl-1H-indol-3-yl)acetamide

268. N-(5-isopropyl-1,3-thiazol-2-yl)-2-(1-methyl-1H-indol-3-yl)acetamide

35 269. N-(5-isopropyl-1,3-thiazol-2-yl)-2-(5-methoxy-1H-indol-3-yl)acetamide

270. N-(5-isopropyl-1,3-thiazol-2-yl)-2-(5-benzyloxy-1H-indol-3-yl)acetamide

271. N-(5-isopropyl-1,3-thiazol-2-yl)-2-(3-methoxy-2-methyl-1H-indol-3-yl)acetamide

272. 2-(1H-indol-3-yl)-N-(5-isopropyl-1,3-thiazol-2-yl)oxoacetamide

5 273. 2-(5-bromo-1H-indol-3-yl)-N-(5-isopropyl-1,3-thiazol-2-yl)acetamide

274. 2-(5-fluoro-1H-indol-3-yl)-N-(5-isopropyl-1,3-thiazol-2-yl)acetamide

10 275. 2-[1-(4-chlorobenzoyl)-5-methoxy-2-methyl-1H-indol-3-yl]-N-(5-isopropyl-1,3-thiazol-2-yl)acetamide

276. 3-(1H-indol-3-yl)-N-(5-isopropyl-1,3-thiazol-2-yl)propanamide

277. 4-(1H-indol-3-yl)-N-(5-isopropyl-1,3-thiazol-2-yl)butanamide

15 278. N-(5-isopropyl-1,3-thiazol-2-yl)-3-(2-thienyl)propanamide

279. N-(5-isopropyl-1,3-thiazol-2-yl)-2-(2-thienyl)acetamide

280. N-(5-isopropyl-1,3-thiazol-2-yl)-2-oxo-2-(2-thienyl)acetamide

20 281. N-(5-isopropyl-1,3-thiazol-2-yl)-2-(3-thienyl)acetamide

282. 2-(5-chloro-1-benzothiophen-3-yl)-N-(5-isopropyl-1,3-thiazol-2-yl)acetamide

25 283. 2-(1-benzothiophen-3-yl)-N-(5-isopropyl-1,3-thiazol-2-yl)acetamide

284. 2-[2-(formylamino)-1,3-thiazol-4-yl]-N-(5-isopropyl-1,3-thiazol-2-yl)-2-(methoxyimino)acetamide

285. 2-{2-[(2-chloroacetyl)amino]-1,3-thiazol-4-yl}-N-(5-isopropyl-1,3-thiazol-2-yl)-2-(methoxyimino)acetamide

30 286. 2-chloro-N-(4-{2-[(5-isopropyl-1,3-thiazol-2-yl)amino]-2-oxoethyl}-1,3-thiazol-2-yl)acetamide

287. ethyl 2-({[2-[(5-isopropyl-1,3-thiazol-2-yl)amino]-2-oxo-1-(1H-pyrazol-3-yl)ethylidene]amino}oxy)acetate

35 288. 2-(2-furyl)-N-(5-isopropyl-1,3-thiazol-2-yl)-2-oxoacetamide

289. 2-(5-bromo-3-pyridinyl)-N-(5-isopropyl-1,3-thiazol-2-yl)acetamide

290. N-(5-isopropyl-1,3-thiazol-2-yl)-2-(7-methoxy-2-oxo-2H-chromen-4-yl)acetamide

291. N-(5-isopropyl-1,3-thiazol-2-yl)-4-phenyl-3-butenamide

292. N-(5-isopropyl-1,3-thiazol-2-yl)-4-oxo-4-(4-methyl-5-phenyl)butanamide

293. N-(5-isopropyl-1,3-thiazol-2-yl)-4-(4-nitrophenyl)butanamide

294. N-(5-isopropyl-1,3-thiazol-2-yl)-4-phenylbutanamide

295. benzyl 4-[(5-isopropyl-1,3-thiazol-2-yl)amino]-4-10 oxobutylcarbamate

296. methyl 5-[(5-isopropyl-1,3-thiazol-2-yl)amino]-5-oxopentanoate

297. 4-(1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl)-N-(5-isopropyl-1,3-thiazol-2-yl)butanamide

298. N-(5-isopropyl-1,3-thiazol-2-yl)-4-(4-methoxy-1-naphthyl)-4-oxobutanimide

299. 3-(2-chlorophenoxy)-N-(5-isopropyl-1,3-thiazol-2-yl)propanamide

300. 3-(4-methylphenoxy)-N-(5-isopropyl-1,3-thiazol-2-yl)propanamide

301. 3-cyclopentyl-N-(5-isopropyl-1,3-thiazol-2-yl)propanamide

302. 3-cyclohexyl-N-(5-isopropyl-1,3-thiazol-2-yl)propanamide

303. N-(5-isopropyl-1,3-thiazol-2-yl)-4-methylpentanamide

304. 3-(4-chlorophenyl)-N-(5-isopropyl-1,3-thiazol-2-yl)propanamide

305. 3-(4-methoxyphenyl)-N-(5-isopropyl-1,3-thiazol-2-yl)propanamide

306. 3-chloro-N-(5-isopropyl-1,3-thiazol-2-yl)propanamide

307. 3-phenyl-N-(5-isopropyl-1,3-thiazol-2-yl)propanamide

308. 2-cyclohexyl-N-(5-isopropyl-1,3-thiazol-2-yl)acetamide

309. N-(5-isopropyl-1,3-thiazol-2-yl)-3-methylbutanamide

310. N-(5-isopropyl-1,3-thiazol-2-yl)-5-oxo-5-35 phenylpentanamide

311. 2-[(5-isopropyl-1,3-thiazol-2-yl)amino]-2-oxo-1-phenylethyl acetate

312. N-(5-isopropyl-1,3-thiazol-2-yl)-2-[4-(1-oxo-1,3-dihydro-2H-isoindol-2-yl)phenyl]propanamide

313. 1-(4-chlorophenyl)-N-(5-isopropyl-1,3-thiazol-2-yl)cyclopentanecarboxamide

5 314. 1-phenyl-N-(5-isopropyl-1,3-thiazol-2-yl)cyclopentanecarboxamide

315. 2-(3-bromo-4-methoxyphenyl)-N-(5-isopropyl-1,3-thiazol-2-yl)acetamide

10 316. 2-(2-nitro-4-trifluoromethylphenyl)-N-(5-isopropyl-1,3-thiazol-2-yl)acetamide

317. 5-cyclohexyl 1-(4-{2-[(5-isopropyl-1,3-thiazol-2-yl)amino]-2-oxoethyl}benzyl) (2S)-2-[(tert-butoxycarbonyl)amino]pentanedioate

15 318. 2-(5,6-dimethyl-1H-benzimidazol-1-yl)-N-(5-isopropyl-1,3-thiazol-2-yl)acetamide

319. 2-[5-(4-chlorophenyl)-2H-1,2,3,4-tetraazol-2-yl]-N-(5-isopropyl-1,3-thiazol-2-yl)acetamide

320. N-(5-isopropyl-1,3-thiazol-2-yl)-2-[5-(1-pyrrolidinyl)-2H-1,2,3,4-tetraazol-2-yl]acetamide

20 321. N-(5-isopropyl-1,3-thiazol-2-yl)-2-(3-methyl-1-benzothiophen-2-yl)acetamide

322. N-(5-isopropyl-1,3-thiazol-2-yl)-4,4-bis(4-methylphenyl)-3-butenamide

25 323. 2-cyclopropyl-N-(5-isopropyl-1,3-thiazol-2-yl)acetamide

324. N-{4-bromo-6-[(5-isopropyl-1,3-thiazol-2-yl)amino]-6-oxohexyl}benzamide

325. 2-cyclopentyl-N-(5-isopropyl-1,3-thiazol-2-yl)acetamide

30 326. benzyl 6-[(5-isopropyl-1,3-thiazol-2-yl)amino]-6-oxohexylcarbamate

327. N~1~~(5-isopropyl-1,3-thiazol-2-yl)-N~4~~(2-propynyl)-2-butenediamide

328. 4-(2,4-dimethylphenyl)-N-(5-isopropyl-1,3-thiazol-2-yl)-4-oxobutanamide

35 329. 4-(4-benzyloxyphenyl)-N-(5-isopropyl-1,3-thiazol-2-yl)-4-oxobutanamide

330. 4-(thiophen-2-yl)-N-(5-isopropyl-1,3-thiazol-2-yl)-4-oxobutanamide

331. benzyl 2-{{(benzyloxy)carbonyl}amino}-5-[(5-isopropyl-1,3-thiazol-2-yl)amino]-5-oxopentanoate

5 332. 4-(1H-indol-3-yl)-N-{3-[(5-isopropyl-1,3-thiazol-2-yl)amino]-3-oxopropyl}butanamide

333. 4-[(5-isopropyl-1,3-thiazol-2-yl)amino]carbonylphenyl 4-chlorobenzenesulfonate

334. N-(5-isopropyl-1,3-thiazol-2-yl)-4-[(2-methoxyanilino)carbonyl]amino)benzamide

10 335. 4-[(2-(isopropylsulfonyl)acetyl)amino]-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide

336. N-(5-isopropyl-1,3-thiazol-2-yl)-4-[(2-(phenylsulfanyl)acetyl)amino]benzamide

15 337. 4-[(diethylamino)sulfonyl]-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide

338. 2-bromo-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide

339. 3,5-difluoro-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide

340. 3-[(2-fluoroanilino)carbonyl]amino)-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide

20 341. N-(5-isopropyl-1,3-thiazol-2-yl)-1-phenyl-5-propyl-1H-pyrazole-4-carboxamide

342. 3-chloro-4-(isopropylsulfonyl)-N-(5-isopropyl-1,3-thiazol-2-yl)-5-(methylsulfanyl)-2-thiophenecarboxamide

25 343. 3-iodo-4-(isopropylsulfonyl)-N-(5-isopropyl-1,3-thiazol-2-yl)-5-(methylsulfanyl)-2-thiophenecarboxamide

344. 2-[(4-chlorophenyl)sulfonylmethyl]-N-(5-isopropyl-1,3-thiazol-2-yl)-4-methyl-1,3-thiazole-5-carboxamide

30 345. 5-(4-chlorophenyl)-N-(5-isopropyl-1,3-thiazol-2-yl)-2-(trifluoromethyl)-3-furamide

346. N-(5-isopropyl-1,3-thiazol-2-yl)-2-(2,3,4,5,6-pentafluorophenyl)acetamide

35 347. N-(5-isopropyl-1,3-thiazol-2-yl)-2-(2-fluorophenyl)acetamide

348. N-(5-isopropyl-1,3-thiazol-2-yl)-2-(2-bromophenyl)acetamide

349. N-(5-isopropyl-1,3-thiazol-2-yl)-2-(2-chlorophenyl)acetamide

350. N-(5-isopropyl-1,3-thiazol-2-yl)-2-(2-nitrophenyl)acetamide

5 351. N-(5-isopropyl-1,3-thiazol-2-yl)-2-(2-trifluoromethylphenyl)acetamide

352. N-(5-isopropyl-1,3-thiazol-2-yl)-2-(2-methoxyphenyl)acetamide

353. N-(5-isopropyl-1,3-thiazol-2-yl)-2-(2,5-dimethoxyphenyl)acetamide

10 354. N-(5-isopropyl-1,3-thiazol-2-yl)-2-(2,5-difluorophenyl)acetamide

355. N-(5-isopropyl-1,3-thiazol-2-yl)-2-(3,4,5-trimethoxyphenyl)acetamide

15 356. N-(5-isopropyl-1,3-thiazol-2-yl)-2-(2,6-dichlorophenyl)acetamide

357. N-(5-isopropyl-1,3-thiazol-2-yl)-2-(2-chloro-6-fluorophenyl)acetamide

358. N-(5-isopropyl-1,3-thiazol-2-yl)-2-(3,5-dimethoxyphenyl)acetamide

20 359. N-(5-isopropyl-1,3-thiazol-2-yl)-2-(3,5-difluorophenyl)acetamide

360. N-(5-isopropyl-1,3-thiazol-2-yl)-2-(2,5-bis-trifluoromethylphenyl)acetamide

25 361. N-(5-isopropyl-1,3-thiazol-2-yl)-2-(4-methylthiophenyl)acetamide

362. N-(5-isopropyl-1,3-thiazol-2-yl)-2-(4-methoxyphenyl)acetamide

363. N-(5-isopropyl-1,3-thiazol-2-yl)-2-(4-bromophenyl)acetamide

30 364. N-(5-isopropyl-1,3-thiazol-2-yl)-2-(4-chlorophenyl)acetamide

365. N-(5-isopropyl-1,3-thiazol-2-yl)-2-(4-fluorophenyl)acetamide

35 366. N-(5-isopropyl-1,3-thiazol-2-yl)-2-(4-nitrophenyl)acetamide

367. N-(5-isopropyl-1,3-thiazol-2-yl)-2-(4-trifluoromethylphenyl)acetamide

368. N-(5-isopropyl-1,3-thiazol-2-yl)-2-(4-methylphenyl)acetamide

369. N-(5-isopropyl-1,3-thiazol-2-yl)-2-(4-dimethylaminophenyl)acetamide

5 370. 2-[1,1'-biphenyl]-4-yl-N-(5-isopropyl-1,3-thiazol-2-yl)acetamide

371. N-(5-isopropyl-1,3-thiazol-2-yl)-2-(3-trifluoromethylphenyl)acetamide

10 372. N-(5-isopropyl-1,3-thiazol-2-yl)-2-(3-bromophenyl)acetamide

373. N-(5-isopropyl-1,3-thiazol-2-yl)-2-(3-chlorophenyl)acetamide

374. N-(5-isopropyl-1,3-thiazol-2-yl)-2-(3-nitrophenyl)acetamide

15 375. N-(5-isopropyl-1,3-thiazol-2-yl)-2-(3-methoxyphenyl)acetamide

376. N-(5-isopropyl-1,3-thiazol-2-yl)-2-(2,4-dinitrophenyl)acetamide

377. N-(5-isopropyl-1,3-thiazol-2-yl)-2-(2,4-20 dichlorophenyl)acetamide

378. N-(5-isopropyl-1,3-thiazol-2-yl)-2-(2,4-difluorophenyl)acetamide

379. N-(5-isopropyl-1,3-thiazol-2-yl)-2-(4-benzyloxy-3-methoxyphenyl)acetamide

25 380. N-(5-isopropyl-1,3-thiazol-2-yl)-2-(3,4-dichlorophenyl)acetamide

381. N-(5-isopropyl-1,3-thiazol-2-yl)-2-(3,4-difluorophenyl)acetamide

382. N-(5-isopropyl-1,3-thiazol-2-yl)-2-(3,4-30 dimethoxyphenyl)acetamide

383. 2-(2,3-dihydro-1H-inden-5-yl)-N-(5-isopropyl-1,3-thiazol-2-yl)acetamide

384. N-(5-isopropyl-1,3-thiazol-2-yl)-1-phenylcyclopropanecarboxamide

35 385. 2-cyclopentyl-N-(5-isopropyl-1,3-thiazol-2-yl)-2-phenylacetamide

386. 2-cyclohexyl-N-(5-isopropyl-1,3-thiazol-2-yl)-2-phenylacetamide

387. N-(5-isopropyl-1,3-thiazol-2-yl)-2,2-diphenylacetamide

388. N-(5-isopropyl-1,3-thiazol-2-yl)-2-(2-nitrophenoxy)acetamide

5 389. N-(5-isopropyl-1,3-thiazol-2-yl)-2-(4-nitrophenyl)propanamide

390. N-(5-isopropyl-1,3-thiazol-2-yl)-2-phenylpropanamide

391. N-(5-isopropyl-1,3-thiazol-2-yl)-2-(4-isobutylphenyl)propanamide

10 392. N-(5-isopropyl-1,3-thiazol-2-yl)-2-oxo-2-phenylacetamide

393. N-(5-isopropyl-1,3-thiazol-2-yl)-3-methyl-2-phenylpentanamide

394. (E, Z)-N-(5-isopropyl-1,3-thiazol-2-yl)-2-phenyl-2-butenamide

15 395. N-(5-isopropyl-1,3-thiazol-2-yl)bicyclo[4.2.0]octa-1,3,5-triene-7-carboxamide

396. N-(5-isopropyl-1,3-thiazol-2-yl)-3-oxo-1-indanecarboxamide

20 397. N-(5-isopropyl-1,3-thiazol-2-yl)-2-phenylbutanamide

398. tert-butyl (1S)-2-[(5-isopropyl-1,3-thiazol-2-yl)amino]-1-methyl-2-oxoethylcarbamate

399. tert-butyl (1S,2S)-1-[(5-isopropyl-1,3-thiazol-2-yl)amino]carbonyl-2-methylbutylcarbamate

25 400. tert-butyl 2-[(5-isopropyl-1,3-thiazol-2-yl)amino]-2-oxoethylcarbamate

401. tert-butyl (1S)-5-amino-1-[(5-isopropyl-1,3-thiazol-2-yl)amino]carbonylpentylcarbamate

402. tert-butyl 4-[(imino{[(4-

30 methylphenyl)sulfonyl]amino}methyl)amino]-1-[(5-isopropyl-1,3-thiazol-2-yl)amino]carbonylbutylcarbamate

403. tert-butyl 1-[(5-isopropyl-1,3-thiazol-2-yl)amino]carbonyl-3-(tritylamino)propylcarbamate

35 404. tert-butyl (1S)-1-(benzyloxymethyl)-2-[(5-isopropyl-1,3-thiazol-2-yl)amino]-2-oxoethylcarbamate

405. tert-butyl (1S)-1-benzyl-2-[(5-isopropyl-1,3-thiazol-2-yl)amino]-2-oxoethylcarbamate

406. *tert*-butyl (1*R*)-2-[(5-isopropyl-1,3-thiazol-2-yl)amino]-2-oxo-1-(benzylthiomethyl)ethylcarbamate

407. benzyl (3*S*)-3-[(*tert*-butoxycarbonyl)amino]-4-[(5-isopropyl-1,3-thiazol-2-yl)amino]-4-oxobutanoate

5 408. *tert*-butyl (2*S*)-2-[(5-isopropyl-1,3-thiazol-2-yl)amino]carbonyl-1-pyrrolidinecarboxylate

409. *tert*-butyl (1*S*)-1-(1*H*-indol-3-ylmethyl)-2-[(5-isopropyl-1,3-thiazol-2-yl)amino]-2-oxoethylcarbamate

410. *tert*-butyl (1*S*)-1-[(5-isopropyl-1,3-thiazol-2-yl)amino]carbonyl-3-(methylsulfanyl)propylcarbamate

10 411. *tert*-butyl (1*S*)-2-benzyloxy-1-[(5-isopropyl-1,3-thiazol-2-yl)amino]carbonylpropylcarbamate

412. *tert*-butyl (1*S*)-1-(4-benzyloxybenzyl)-2-[(5-isopropyl-1,3-thiazol-2-yl)amino]-2-oxoethylcarbamate

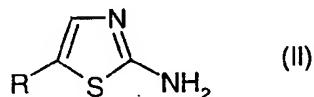
15 413. *tert*-butyl (1*S*)-1-[(5-isopropyl-1,3-thiazol-2-yl)amino]carbonyl-2-methylpropylcarbamate

414. *tert*-butyl (1*S*)-1-[(5-isopropyl-1,3-thiazol-2-yl)amino]carbonyl-3-methylbutylcarbamate

415. benzyl (4*S*)-4-[(*tert*-butoxycarbonyl)amino]-5-[(5-isopropyl-1,3-thiazol-2-yl)amino]-5-oxopentanoate;

20 and the pharmaceutically acceptable salts thereof.

The compounds of formula (I) object of the present invention and the salts thereof can be obtained, for 25 instance, by a process comprising reacting a compound of formula (II)



with a compound of formula (III)



30 wherein R and R_1 are as defined above and X is hydroxy or a suitable leaving group; and, if desired, converting a 2-amino-1,3-thiazole derivative of formula (I) into another such derivative of formula (I), and/or into a salt thereof.

Examples of specific compounds of formula (III) wherein X is a suitable leaving group are those wherein X represents a halogen atom, preferably chlorine or bromine.

5 It is clear to the man skilled in the art that if the compound of formula (I), prepared according to the above process is obtained as an admixture of isomers, its separation into the single isomers according to conventional techniques is still within the scope of the
10 present invention.

Likewise, the conversion into the free compound (I) of a corresponding salt thereof, according to well-known procedures in the art, is still within the scope of the invention.

15

The above process is an analogy process which can be carried out according to well known methods.

The reaction between a compound of formula (II) and a carboxylic acid of formula (III) wherein X is a hydroxy group, can be carried out in the presence of a coupling agent or a polymer supported coupling agent such as, for instance, carbodiimide, i.e. 1,3-dicyclohexylcarbodiimide, 1,3-diisopropylcarbodiimide, 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide, or N-Cyclohexylcarbodiimide N'-methylpolystyrene in a suitable solvent such as, for instance, dichloromethane, chloroform, tetrahydrofuran, diethyl ether, 1,4-dioxane, acetonitrile, toluene, or N,N-dimethylformamide at a temperature ranging from about -10°C to reflux for a suitable time, i.e. from about 30 min. to
30 about 96 hours.

The reaction between a compound of formula (II) and a compound of formula (III) can be also carried out, for example, by a mixed anhydride method, using an alkyl chloroformate, such as ethyl, iso-butyl, or iso-propyl chloroformate, in the presence of a tertiary base, such as triethylamine, N,N-diisopropylethylamine or pyridine, in a suitable solvent such as, for instance, toluene, dichloromethane, chloroform, tetrahydrofuran, acetonitrile,

diethyl ether, 1,4-dioxane, or N,N-dimethylformamide, at a temperature ranging from about -30°C to room temperature. The reaction between a compound of formula (II) and a carboxylic acid derivative of formula (III) wherein X is a 5 suitable leaving group can be carried out in the presence of a tertiary base, such as triethylamine, N,N-diisopropylethylamine or pyridine, in a suitable solvent, such as toluene, dichloromethane, chloroform, diethyl ether, tetrahydrofuran, acetonitrile, or N,N-10 dimethylformamide, at a temperature ranging from about -10°C to reflux.

Also the optional conversion of a compound of formula (I) into another compound of formula (I) can be carried out 15 according to known methods.

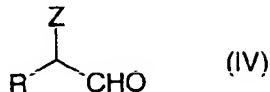
As an example, the nitro group of a compound of formula (I) may be converted into an amino group by treatment, for example, with stannous chloride in concentrated hydrochloric acid and by using, if necessary, an organic 20 solvent such as acetic acid, 1,4-dioxane and tetrahydrofuran, at a temperature varying between room temperature and about 100°C.

Likewise, an alkylthio or an arylthio group may be converted into the corresponding alkylsulfonyl and 25 arylsulfonyl group by reaction, for example, with m-chloroperbenzoic acid in a suitable solvent such as dichloromethane or chloroform, at a temperature varying between about -5°C and room temperature.

The optional salification of a compound of formula (I) or 30 the conversion of a salt into the free compound as well as the separation of a mixture of isomers into the single isomers may be carried out by conventional methods.

The compounds of formula (II) and (III) according to the 35 process object of the present invention are known compounds or can be obtained according to known methods.

For example, a compound of formula (II) wherein R is as defined above can be obtained by reacting a compound of formula (IV)



5 wherein Z is a bromine or chlorine atom, with thiourea in a suitable solvent such as methanol, ethanol, tetrahydrofuran, 1,4-dioxane or toluene, at a temperature varying between room temperature and reflux, for a suitable time ranging from about 1 hour to about 24 hours.

10 A compound of formula (III) wherein X is a leaving group as defined above can be obtained according to conventional techniques from the corresponding carboxylic acids of formula (III) wherein X is hydroxy.

When preparing the compounds of formula (I) according to
15 the process object of the present invention, optional functional groups within both the starting materials or the intermediates thereof, which could give rise to unwanted side reactions, need to be properly protected according to conventional techniques.

20 Likewise, the conversion of these latter into the free deprotected compounds may be carried out according to known procedures.

Pharmacology

25 The compounds of formula (I) are active as cdk/cyclin inhibitors as they gave positive results when tested according to the following procedure.

30 The inhibiting activity of putative cdk/cyclin¹ inhibitors and the potency of selected compounds was determined through a method of assay based on the use of the MultiScreen-PH 96 well plate (Millipore), in which a phosphocellulose filter paper was placed at each well bottom allowing binding of positive charged substrate after
35 a washing/filtration step.

When a radioactivity labelled phosphate moiety was transferred by the ser/threo kinase to the filter-bound histone, light emitted was measured in a scintillation counter.

5 The inhibition assay of cdk2/Cyclin A activity was performed according to the following protocol:

Kinase reaction: 1.5 μ M histone H1 substrate, 25 μ M ATP (0.5 μ Ci $\text{P}^{33}\gamma$ -ATP), 30 ng Cyclin A/cdk2 complex, 10 μ M 10 inhibitor in a final volume of 100 μ l buffer (TRIS HCl 10 mM pH 7.5, MgCl_2 , 10 mM, 7.5 mM DTT) were added to each well of a 96 U bottom well plate. After 10 min at 37 °C incubation, reaction was stopped by 20 μ l EDTA 120 mM.

15 **Capture:** 100 μ l were transferred from each well to MultiScreen plate, to allow substrate binding to phosphocellulose filter. Plates were then washed 3 times with 150 μ l/well PBS $\text{Ca}^{++}/\text{Mg}^{++}$ free and filtered by MultiScreen filtration system.

20 **Detection:** filters were allowed to dry at 37°C, then 100 μ l/well scintillant were added and ^{33}P labelled histone H1 was detected by radioactivity counting in the Top-Count instrument.

25 **Results:** data were analysed and expressed as % inhibition referred to total activity of enzyme (=100%). All compounds showing inhibition \geq 50 % were further analysed in order to study and define potency (IC50) as 30 well as the kinetic-profile of inhibitor through Ki calculation.

IC50 determination: the protocol used was the same described above, where inhibitors were tested at concentrations ranging from 0.0045 to 10 μ M. Experimental 35 data were analyzed by the computer program GraphPad Prizm.

Ki calculation: either the concentration of ATP and histone H1 substrate were varied: 4, 8, 12, 24, 48 μ M for ATP (containing proportionally diluted $P^{32}\gamma$ -ATP) and 0.4, 0.8, 1.2, 2.4, 4.8 μ M for histone were used in absence and 5 presence of two different, properly chosen inhibitor concentrations.

Experimental data were analysed by the computer program SigmaPlot for Ki determination, using a random bireactant system equation:

$$10 \quad V_{max} \quad \frac{(A)(B)}{aK_A K_B}$$
$$V = \frac{1 + \frac{(A)}{K_A} + \frac{(B)}{K_B} + \frac{(A)(B)}{aK_A K_B}}{1 + \frac{(A)}{K_A} + \frac{(B)}{K_B}}$$

15 where A=ATP and B=histone H1.

Following the method above described, a representative compound of formula (I) of the invention, which is 2-[4-(dimethylamino)phenyl]-N-(5-isopropyl-1,3-thiazol-2-yl)acetamide, showed an inhibiting activity towards the 20 cdk2/cyclin A complex corresponding to 0.1 μ M (Ki).

In addition, the inhibiting activity of putative cdk/cyclin 25 inhibitors and the potency of selected compounds was determined through a method of assay based on the use of a SPA (Scintillation Proximity Assay) 96 well plate assay. The assay is based on the ability of streptavidin coated SPA beads to capture a biotinylated peptide derived from a phosphorylation site of histone.

30 When a radioactivity labelled phosphate moiety was transferred by the ser/threo kinase to the biotinylated histone peptide, light emitted was measured in a scintillation counter.

35 The inhibition assay of cdk5/p25 activity was performed according to the following protocol:

Kinase reaction: 1.0 μ M biotinylated histone peptide substrate, 0.25 uCi P33g-ATP, 4 nM cdk2/p25 complex, 0-100 μ M inhibitor in a final volume of 100 μ l buffer (Hepes 20 mM pH 7.5, MgCl₂ 15 mM, 1 mM DTT) were added to each well 5 of a 96 U bottom well plate. After 20 min at 37 °C incubation, the reaction was stopped by the addition of 500 ug SPA beads in phosphate-buffered saline containing 0.1% Triton X-100, 50 μ M ATP and 5 mM EDTA. The beads were allowed to settle, and the radioactivity incorporated in 10 the 33P-labelled peptide was detected in a Top Count scintillation counter.

Results: Data were analyzed and expressed as % Inhibition using the formula:

$$15 \quad 100 \times (1 - (\text{Unknown} - \text{Bkgd}) / (\text{Enz. Control} - \text{Bkgd}))$$

IC₅₀ values were calculated using a variation of the four parameter logistics equation:

$$Y = 100 / [1 + 10^{((\text{LogEC50} - X) * \text{Slope})}]$$

20

Where X = log(μ M) and Y = % Inhibition.

The compounds of formula (I) are therefore useful to restrict the unregulated proliferation of tumor cells, 25 hence in therapy in the treatment of various tumors such as, for instance, carcinomas, e.g. mammary carcinoma, lung carcinoma, bladder carcinoma, colon carcinoma, ovary and endometrial tumors, sarcomas, e.g. soft tissue and bone sarcomas, and the hematological malignancies such as, e.g., 30 leukemias.

In addition, the compounds of formula (I) are also useful in the treatment of other cell proliferative disorders such as psoriasis, vascular smooth cell proliferation associated with atherosclerosis and post-surgical stenosis and 35 restenosis and in the treatment of Alzheimer's disease.

The compounds of the present invention can be administered either as single agents or, alternatively, in combination with known anticancer treatments such as radiation therapy or chemotherapy regimen in combination with cytostatic or 5 cytotoxic agents.

As an example, the above compounds can be administered in combination with one or more chemotherapeutic agents such as, for instance, taxane, taxane derivatives, CPT-11, camptothecin derivatives, anthracycline glycosides, e.g. 10 doxorubicin or epirubicin, etoposide, navelbine, vinblastine, carboplatin, cisplatin and the like, optionally within liposomal formulations thereof.

The compounds of formula (I) of the present invention, 15 suitable for administration to a mammal, e.g. to humans, can be administered by the usual routes and the dosage level depends upon the age, weight, conditions of the patient and the administration route.

For example, a suitable dosage adopted for oral 20 administration of a compound of formula (I) may range from about 10 to about 500 mg pro dose, from 1 to 5 times daily. The compounds of the invention can be administered in a variety of dosage forms, e.g. orally, in the form of tablets, capsules, sugar or film coated tablets, liquid 25 solutions or suspensions; rectally in the form of suppositories; parenterally, e.g. intramuscularly, or by intravenous and/or intrathecal and/or intraspinal injection or infusion.

30 The present invention also includes pharmaceutical compositions comprising a compound of formula (I), or a pharmaceutically acceptable salt thereof, in association with a pharmaceutically acceptable excipient (which can be a carrier or a diluent).

35 The pharmaceutical compositions containing the compounds of the invention are usually prepared following conventional methods and are administered in a pharmaceutically suitable form.

For example, the solid oral forms may contain, together with the active compound, diluents, e.g. lactose, dextrose, saccharose, sucrose, cellulose, corn starch or potato starch; lubricants, e.g. silica, talc, stearic acid, 5 magnesium or calcium stearate, and/or polyethylene glycols; binding agents, e.g. starches, arabic gum, gelatine, methylcellulose, carboxymethylcellulose or polyvinyl pyrrolidone; disaggregating agents, e.g. a starch, alginic acid, alginates or sodium starch glycolate; effervescent 10 mixtures; dyestuffs; sweeteners; wetting agents such as lecithin, polysorbates, laurylsulphates; and, in general, non-toxic and pharmacologically inactive substances used in pharmaceutical 15 formulations. Said pharmaceutical preparations may be manufactured in known manner, for example, by means of mixing, granulating, tabletting, sugar-coating, or film-coating processes.

The liquid dispersions for oral administration may be e.g. syrups, emulsions and suspensions.

The syrups may contain as carrier, for example, saccharose 20 or saccharose with glycerine and/or mannitol and/or sorbitol.

The suspensions and the emulsions may contain as carrier, for example, a natural gum, agar, sodium alginate, pectin, methylcellulose, carboxymethylcellulose, or polyvinyl 25 alcohol.

The suspension or solutions for intramuscular injections may contain, together with the active compound, a pharmaceutically acceptable carrier, e.g. sterile water, olive oil, ethyl oleate, glycols, e.g. propylene glycol, 30 and, if desired, a suitable amount of lidocaine hydrochloride. The solutions for intravenous injections or infusions may contain as carrier, for example, sterile water or preferably they may be in the form of sterile, aqueous, isotonic saline solutions or they may contain as a 35 carrier propylene glycol.

The suppositories may contain together with the active compound a pharmaceutically acceptable carrier, e.g. cocoa

butter, polyethylene glycol, a polyoxyethylene sorbitan fatty acid ester surfactant or lecithin.

The following examples illustrate but do not limit the 5 present invention.

Example 1

Preparation of Ethyl 3-[(5-bromo-1,3-thiazol-2-yl)amino]-3-oxopropanoate

10 Ethyl malonyl chloride (0.88 ml; 6.99 mmol) was added to a mixture of 2-amino-5-bromothiazole hydrobromide (1.30 g; 5.00 mmol) and Et₃N (2.08 ml; 14.94 mmol) in THF (6 ml) at 0-5°C. The mixture was stirred at room temperature overnight, then the reaction was quenched with potassium 15 sarcosinate (0.25 g; 2.00 mmol) and water (12 ml). The product was isolated by filtration as a white solid (0.75 g, 51%): m.p. 165-166°C.

¹H-NMR (CDCl₃) δ ppm: 10.80 (bs, 1H, CONH); 7.38 (s, 1H, thiazole CH); 4.28 (q, J = 7.3 Hz, 2H, COOCH₂CH₃); 3.56 (s, 2H, COCH₂CO); 1.32 (t, J = 7.3 Hz, 2H, COOCH₂CH₃).

Analogously, the following products can be prepared:

N-(5-bromo-1,3-thiazol-2-yl)-2-phenyl-acetamide
m.p. 206-207°C

¹H-NMR (DMSO-d₆) δ ppm: 3.76 (s, 2H, COCH₂Ph); 7.2-7.3 (m, 25 5H, Ph); 7.54 (s, 1H, thiazole CH); 12.80 (bs, 1H, CONH); N-(5-bromo-1,3-thiazol-2-yl)-benzamide
m.p. 126-128°C

¹H-NMR (DMSO-d₆) δ ppm: 12.90 (bs, 1H, CONH); 8.07, 7.93 (m, 2H, o-Ph hydrogens); 7.63 (s, 1H, thiazole CH); 7.62, 7.53, 30 7.48 (m, 3H, m- and p-Ph hydrogens);

Ethyl 4-[(5-bromo-1,3-thiazol-2-yl)amino]-4-oxobutanoate.

Example 2

Preparation of N-(5-Bromo-thiazol-2-yl)-3-hydroxy-propionamide

A mixture of LiBH₄ (44 mg, 2.02 mmol), ethyl 3-[(5-bromo-1,3-thiazol-2-yl)amino]-3-oxopropanoate (340 mg, 1.16 mmol), methanol (0.082 ml, 2.02 mmol), and Et₂O (50 ml) was refluxed for 20 min. The reaction was quenched with 1 N hydrochloric acid with ice-cooling.

5 The mixture was then diluted with water and extracted with dichloromethane. The extract was dried and the solvent was evaporated under reduced pressure. Purification by silica gel chromatography (dichloromethane/methanol=98:2 and then 10 95:5) yielded the title compound as a white solid (0.17 g; 52%).

m.p. 182-184°C (dec.)

¹H-NMR (CDCl₃) δ ppm: 10.20 (bs, 1H, CONH); 7.35 (s, 1H, thiazole CH); 4.04 (t, J = 5.4 Hz, 2H, COCH₂CH₂OH); 2.74 15 (t, J = 5.4 Hz, 2H, COCH₂CH₂OH).

Analogously, starting from the corresponding ester derivative the following product can be prepared:
N-(5-Bromo-1,3-thiazol-2-yl)-4-hydroxybutanamide.

20

Example 3

Preparation of N-(5-Bromo-thiazol-2-yl)-2-ethoxy-acetamide

EDCI (0.53 g, 2.78 mmol) was added to a solution of ethoxyacetic acid (0.29 g, 2.78 mmol) in CH₂Cl₂ (5 ml) 25 under ice-cooling.

After stirring for 1 h, a solution of 2-amino-5-bromothiazole hydrobromide (0.60 g, 2.31 mmol) and diisopropylethylamine (0.40 ml, 2.34 mmol) in CH₂Cl₂ (5 ml) was added dropwise, and the entire mixture was kept at 0°C 30 for 1 h, then at room temperature overnight.

The solution was evaporated and the residue partitioned between ethyl acetate and water. The ethyl acetate layer was further washed with water, 5% citric acid, water, saturated sodium bicarbonate, and water.

35 Drying over sodium sulfate and evaporation gave a solid which was triturated with isopropyl ether to give the title compound as a beige solid (0.43 g; 70%)

m.p. 100-102°C

¹H-NMR (CDCl₃) δ ppm: 9.64 (bs, 1H, CONH); 7.38 (s, 1H, thiazole CH); 4.16 (s, 2H, COCH₂O); 3.65 (q, J = 6.8 Hz, 2H, OCH₂CH₃); 1.29 (t, J = 6.8 Hz, 3H, OCH₂CH₃).

5 Analogously, the following products can be prepared:

tert-butyl 3-[(5-bromo-1,3-thiazol-2-yl)amino]-3-oxopropylcarbamate;

Benzyl 4-[(5-bromo-1,3-thiazol-2-yl)amino]-4-oxobutylcarbamate;

10 tert-butyl 4-{2-[(5-isopropyl-1,3-thiazol-2-yl)amino]-2-oxoethyl}phenylcarbamate

tert-butyl 4-[(5-isopropyl-1,3-thiazol-2-yl)amino]carbonylphenylcarbamate

tert-butyl 4-{2-[(5-isopropyl-1,3-thiazol-2-yl)amino]-2-oxoethyl}-1,3-thiazol-2-ylcarbamate;

N-(5-bromo-1,3-thiazol-2-yl)-2-bromoacetamide;

N-(5-isopropyl-1,3-thiazol-2-yl)-2-bromoacetamide;

2-N-[2-(3-pyridyl)-acetyl-amino]-5-bromo-thiazole

m.p. 232-235°C

20 ¹H-NMR (DMSO-d₆): 3.82 (s, 2H, COCH₂Ph); 7.34 (dd, J=4.4, 7.7 Hz, 1H, H₅ Py); 7.55 (s, 1H, thiazole CH); 7.71 (ddd, J=1.6, 2.2, 7.7 Hz, 1H, H₄ Py); 8.45 (dd, J=1.6, 4.9 Hz, 1H, H₆ Py); 8.49 (d, J=2.2 Hz, 1H, H₂ Py); 12.65 (s, 1H, CONH);

25 2-N-[2-(3-pyridyl)-acetyl-amino]-5-isopropyl-thiazole

m.p. 178-180°C (dec.)

¹H-NMR (DMSO-d₆) δ ppm: 12.20 (bs, 1H, CONH); 8.45, 7.7, 7.35 (m, 4H, Py); 7.17 (s, 1H, thiazole CH); 3.78 (s, 2H, COCH₂); 3.14 (m, 1H, CH(Me)₂); 1.22 (d, 6H, CHMe₂);

30 N-(5-bromo-1,3-thiazol-2-yl)-2-(3-hydroxyphenyl)acetamide;
N-(5-isopropyl-1,3-thiazol-2-yl)-2-(3-hydroxyphenyl)acetamide

m.p. 206-208°C.

¹H-NMR (DMSO-d₆) δ ppm: 12.1 (bs, 1H, CONH); 9.34 (s, 1H,

35 OH); 7.14 (s, 1H, thiazole CH); 7.1 (t, 1H, H₅ Ph); 6.6-6.7

(m, 3H, H2, H4, H6 Ph); 3.6 (s, 2H, COCH₂); 3.08 (ept, 1H, CHMe₂); 1.22 (d, 6H, CHMe₂);
 N-(5-bromo-1,3-thiazol-2-yl)-2-(3-methoxyphenyl)acetamide;
 N-(5-isopropyl-1,3-thiazol-2-yl)-2-(3-
 5 methoxyphenyl)acetamide
 m.p. 97-98°C.
¹H-NMR (DMSO-d₆) δ ppm: 12.12 (s, 1H, CONH); 7.21 (dd, 1H, H5 Ph); 7.14 (d, 1H, thiazole CH); 6.87 (m, 2H, H2, H6 Ph); 6.81 (ddd, 1H, H4 Ph); 3.72 (s, 3H, OMe); 3.67 (s, 2H, COCH₂); 3.07 (m, 1H, CHMe₂); 1.22 (d, 6H, CHMe₂);
 N-(5-bromo-1,3-thiazol-2-yl)-2-(3-chlorophenyl)acetamide;
 N-(5-isopropyl-1,3-thiazol-2-yl)-2-(3-chlorophenyl)acetamide
 m.p. 116-118°C.
¹H-NMR (CDCl₃) δ ppm: 11.8 (bs, 1H, CONH); 7.32 (s, 1H, H2 Ph); 7.24 (m, 3H, H4, H5, H6 Ph); 7.04 (s, 1H, thiazole CH); 3.76 (s, 2H, COCH₂); 3.13 (m, 1H, CHMe₂); 1.31 (d, 6H, CHMe₂);
 N-(5-bromo-1,3-thiazol-2-yl)-2-(4-hydroxyphenyl)acetamide;
 N-(5-isopropyl-1,3-thiazol-2-yl)-2-(4-
 20 hydroxyphenyl)acetamide
¹H-NMR (DMSO-d₆) δ ppm: 12.07 (bs, 1H, CONH); 9.33 (sb, 1H, OH); 7.17-6.7 (m, 5H, Ar+ CHthiazole); 3.60 (s, 2H, COCH₂); 3.1 (m, 1H, CHMe₂); 1.23 (d, 6H, CHMe₂);
 N-(5-bromo-1,3-thiazol-2-yl)-2-(3,4-
 25 dihydroxyphenyl)acetamide; ||
 N-(5-isopropyl-1,3-thiazol-2-yl)-2-(3,4-
 dihydroxyphenyl)acetamide ||
 m.p. 168-169°C.
¹H-NMR (DMSO-d₆) δ ppm: 12.01 (bs, 1H, CONH); 8.79 (sb, 2H, 2
 30 OH); 7.12 (s, 1H, thiazole CH); 6.69 (d, 1H, H2 Ph); 6.63 (d, 1H, H5 Ph); 6.52 (dd, 1H, H6 Ph); 3.48 (s, 2H, COCH₂); 3.06 (m, 1H, CHMe₂); 1.22 (d, 6H, CHMe₂);
 N-(5-bromo-1,3-thiazol-2-yl)-2-(4-hydroxy-3-
 methoxyphenyl)acetamide;
 35 N-(5-isopropyl-1,3-thiazol-2-yl)-2-(4-hydroxy-3-
 methoxyphenyl)acetamide
 m.p. 115-116°C.

¹H-NMR (DMSO-d₆) δ ppm: 12.0 (bs, 1H, CONH); 8.80 (s, 1H, OH); 7.12 (d, 1H, thiazole CH); 6.88 (s, 1H, H2 Ph); 6.68 (m, 2H, H5, H6 Ph); 3.73 (s, 3H, OMe); 3.56 (s, 2H, COCH₂); 3.07 (m, 1H, CHMe₂); 1.22 (d, 6H, CHMe₂);

5 N-(5-bromo-1,3-thiazol-2-yl)-2-(4-methoxyphenyl)acetamide; N-(5-isopropyl-1,3-thiazol-2-yl)-2-(4-methoxyphenyl)acetamide
m.p. 129-130°C.

¹H-NMR (DMSO-d₆) δ ppm: 12.08 (s, 1H, CONH); 7.21 (dd, 2H, 10 H2, H6 Ph); 7.13 (d, 1H, thiazole CH); 6.87 (dd, 2H, H3, H5 Ph); 3.70 (s, 3H, OMe); 3.62 (s, 2H, COCH₂); 3.06 (m, 1H, CHMe₂); 1.22 (d, 6H, CHMe₂);
N-(5-isopropyl-1,3-thiazol-2-yl)-2-phenyl-acetamide
m.p. 135-137°C

15 ¹H-NMR (DMSO-d₆) δ ppm: 12.20 (bs, 1H, CONH); 7.29 (m, 5H, Ph); 7.13 (s, 1H, thiazole CH); 3.70 (s, 2H, COCH₂); 3.07 (m, 1H, CHMe₂); 1.22 (d, 6H, CHMe₂);
2-[3-(3-chloropropoxy)phenyl]-N-(5-isopropyl-1,3-thiazol-2-yl)acetamide

20 m.p. 91-92°C

¹H-NMR (DMSO-d₆) δ ppm: 12.08 (bs, 1H, CONH); 7.21 (t, 1H, H5 Ph); 7.13 (s, 1H, thiazole CH); 6.8-6.9 (m, 3H, H2, H4, H6 Ph); 4.05 (t, 2H, OCH₂CH₂CH₂Cl); 3.77 (t, 2H, OCH₂CH₂CH₂Cl); 3.67 (s, 2H, COCH₂); 3.07 (ept, 1H, CHMe₂); 2.14 (quint, 2H, 25 OCH₂CH₂CH₂Cl); 1.22 (d, 6H, CHMe₂); and
2-[3-(2-chloroethoxy)phenyl]-N-(5-isopropyl-1,3-thiazol-2-yl)acetamide
m.p. 134-135°C

¹H-NMR (DMSO-d₆) δ ppm: 12.09 (bs, 1H, CONH); 7.22 (t, 1H, H5 30 Ph); 7.13 (s, 1H, thiazole CH); 6.8-6.9 (m, 3H, H2, H4, H6 Ph); 4.2 (t, 2H, OCH₂CH₂Cl); 3.91 (t, 2H, OCH₂CH₂Cl); 3.67 (s, 2H, COCH₂); 3.07 (ept, 1H, CHMe₂); 1.22 (d, 6H, CHMe₂).

Example 4

35 Preparation of N-(5-bromo-thiazol-2-yl)-4-sulfamoyl-benzamide.

To a mixture of 4-sulfamoylbenzoic acid (1.0 g, 4.97 mmol), Et₃N (1.5 ml, 10.78 mmol), DMF (5 ml) and THF (5 ml) isobutyl chloroformate (0.70 ml, 5.36 mmol) was added dropwise at -10°C.

5 After stirring for 1 h, a solution of 2-amino-5-bromothiazole hydrobromide (1.55 g, 5.96 mmol) and Et₃N (0.83 ml, 5.96 mmol) in DMF (6 ml) and THF (4 ml) was added dropwise to the mixture at the same temperature.

10 The resulting mixture was gradually warmed to room temperature over a period of 3 h and then concentrated by evaporation of the solvent in vacuo. To the resultant residue AcOEt and 5% aqueous NaHCO₃ were added. The separated organic phase was washed with water, dried over anhydrous Na₂SO₄, and concentrated under reduced pressure.

15 The residual solid was purified by flash chromatography (dichloromethane/methanol/30% aqueous ammonia=95:5:0.5) to afford the title compound as a yellow solid (0.77 g, 43%) m.p. 268-270°C

¹H-NMR (DMSO-d₆) δ ppm: 7.54 (s, 2H, SO₂NH₂); 7.67 (s, 1H, thiazole CH); 7.94 (d, J=8.8 Hz, 2H, H₃ and H₅ Ph); 8.21 (d, J=8.8 Hz, 2H, H₂ and H₆ Ph); 13.10 (bs, 1H, CONH).

Analogously, the following product can be prepared:

N-(5-isopropyl-thiazol-2-yl)-4-sulfamoyl-benzamide
m.p. 222-224°C.

25 ¹H-NMR (DMSO-d₆) δ ppm: 12.65 (bs, 1H, CONH); 8.18 (dd, 2H, H₂, H₆ Ph); 7.92 (dd, 2H, H₃, H₅ Ph); 7.51 (s, 2H, SO₂NH₂); 7.25 (s, 1H, thiazole CH); 3.13 (m, 1H, CHMe₂); 1.28 (d, 6H, CHMe₂).

30 **Example 5**

Preparation of 4-amino-N-(5-bromo-1,3-thiazol-2-yl)butanamide hydrobromide

A solution (1.3 ml) of hydrogen bromide in glacial acetic acid (33%) was added to benzyl 4-[(5-bromo-1,3-thiazol-2-yl)amino]-3-oxobutylcarbamate (0.72 g, 1.81 mmol) and the mixture was stirred at room temperature for 1 h.

Ether was added and the solid was filtered and washed with ether. The crude product was recrystallized from MeOH/ether to afford the title compound as a beige solid (0.38 g, 61%), m.p. 211-213°C (dec.)

5 $^1\text{H-NMR}$ (DMSO- d_6) δ ppm: 1.84 (m, 2H, $\text{COCH}_2\text{CH}_2\text{CH}_2\text{NH}_2$); 2.53 (t, $J=6.8$ Hz, 2H, $\text{COCH}_2\text{CH}_2\text{CH}_2\text{NH}_2$); 2.81 (m, 2H, $\text{COCH}_2\text{CH}_2\text{CH}_2\text{NH}_2$); 7.68 (bs, 3H, NH_3^+); 12.42 (s, 1H, CONH).

Example 6

10 Preparation of 3-amino-N-(5-bromo-1,3-thiazol-2-yl)propionamide hydrochloride

A solution 3.6 N HCl in isopropanol (14 ml) was added to tert-butyl 3-[(5-bromo-1,3-thiazol-2-yl)amino]-4-oxopropylcarbamate (0.90 g, 2.57 mmol) and the mixture was 15 stirred at room temperature overnight. The solvent was evaporated and the residual solid was triturated in ether, filtered and dried in vacuo to afford the title compound as a white solid (0.73 g, quantitative yield)
m.p. 255°C ca. (dec.)

20 $^1\text{H-NMR}$ (DMSO- d_6) δ ppm: 2.83 (t, $J=6.8$ Hz, 2H, $\text{COCH}_2\text{CH}_2\text{NH}_2$); 3.07 (q, $J=6.4$ Hz, 2H, $\text{COCH}_2\text{CH}_2\text{NH}_2$); 7.55 (s, 1H, thiazole CH); 7.96 (bs, 3H, NH_3^+); 12.58 (s, 1H, CONH).

Analogously, the following compounds can be prepared:

25 2-(4-aminophenyl)-N-(5-isopropyl-1,3-thiazol-2-yl)acetamide
 $^1\text{H-NMR}$ (DMSO- d_6) δ ppm: 1.22 (d, 6H, CHMe_2); 3.07 (m, 1H, CHMe_2); 3.47 (s, 2H, COCH_2); 4.94 (s, 2H, NH_2); 6.48 (m, 2H, H3, H5 Ph); 6.93 (m, 2H, H2, H6 Ph); 7.12 (d, 1H, CH thiazole); 12.00 (s, 1H, CONH).

30 4-amino-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide
 $^1\text{H-NMR}$ (DMSO- d_6) δ ppm: 1.29 (d, 6H, CHMe_2); 3.12 (m, 1H, CHMe_2); 6.58 (m, 2H, H3, H5 Ph); 7.18 (d, 1H, CH thiazole); 7.82 (m, 2H, H2, H6 Ph); 12.80 (bs, 1H, CONH).

35 2-(2-amino-1,3-thiazol-4-yl)-N-(5-isopropyl-1,3-thiazol-2-yl)acetamide

m.p. 204-206°C ca. (dec.)

¹H-NMR (DMSO-d₆) δ ppm: 1.24 (d, 6H, CHMe₂); 3.10 (m, 1H, CHMe₂); 3.54 (s, 2H, COCH₂); 6.30 (s, 1H, H5 thiazole); 6.88 (s, 2H, NH₂); 7.13 (s, 1H, H4 thiazole); 11.90 (s, 1H, CONH).

5

Example 7**Preparation of N-(5-isopropyl-1,3-thiazol-2-yl)-butanamide**

Triethylamine (0.97 ml; 6.34 mmol) and butanoyl chloride (0.52 ml; 5.07 mmol) were added in this order to a solution 10 of 2-amino-5-isopropyl-1,3-thiazole (0.6 g; 4.23 mmol) in dichloromethane (8 ml), cooled to -5°C.

The reaction mixture was stirred at -5°C for 2 hours and then warmed to room temperature. After additional 4 hours, 15 the organic layer was washed with water, saturated sodium bicarbonate, 1N hydrochloric acid, brine, dried over sodium sulfate and evaporated. The residue was recrystallized from cyclohexane to yield 0.45 g (50%) of the title compound as a colourless solid (m.p. 95-97°C)

¹H-NMR (DMSO-d₆) δ ppm: 11.82 (s, 1H, CONH); 7.11 (s, 1H, thiazole CH); 3.08 (m, 1H, CHMe₂); 2.34 (t, J = 7.1 Hz, 2H, COCH₂CH₂CH₃); 1.58 (m, 2H, COCH₂CH₂CH₃); 1.23 (d, J = 6.6 Hz, 6H, (CH₃)₂CH); 0.87 (t, J = 7.1 Hz, 3H, COCH₂CH₂CH₃).

Analogously, the following compounds can be prepared:

25 N-(5-bromo-1,3-thiazol-2-yl)-butanamide

m.p. 163-164°C

¹H-NMR (DMSO-d₆) δ ppm: 12.27 (bs, 1H, CONH); 7.50 (s, 1H, thiazole CH); 2.39 (t, 2H, COCH₂CH₂CH₃); 1.59 (m, 2H, COCH₂CH₂CH₃); 0.87 (t, 3H, COCH₂CH₂CH₃);

30 N-(5-chloro-1,3-thiazol-2-yl)-butanamide

m.p. 170-171°C

¹H-NMR (DMSO-d₆) δ ppm: 12.25 (bs, 1H, CONH); 7.46 (s, 1H, thiazole CH); 2.38 (t, 2H, COCH₂CH₂CH₃); 1.59 (m, 2H, COCH₂CH₂CH₃); 0.87 (t, 3H, COCH₂CH₂CH₃);

35 N-(5-phenyl-1,3-thiazol-2-yl)-butanamide

m.p. 183-184°C

1H-NMR (DMSO-d₆) δ ppm: 12.13 (s, 1H, CONH), 7.84 (s, 1H, thiazole CH); 7.58 (d, J = 6.8 Hz, 2H, o-Ph hydrogens); 7.39 (dd, J = 6.8 and 7.8 Hz, 2H, m-Ph hydrogens); 7.28 (t, J = 7.8 Hz, 1H, p-Ph hydrogens); 2.41 (t, J = 7.3 Hz, 2H, 5 COCH₂CH₂CH₃); 1.61 (m, 2H, COCH₂CH₂CH₃); 0.89 (t, J = 7.3 Hz, 3H, COCH₂CH₂CH₃);
N-(5-nitro-1,3-thiazol-2-yl)-butanamide
m.p. 175-176°C

1H-NMR (DMSO-d₆) δ ppm: 13.02 (s, 1H, CONH); 8.60 (s, 1H, thiazole CH); 2.48 (t, J = 7.3 Hz, 2H, COCH₂CH₂CH₃); 1.62 (m, 2H, COCH₂CH₂CH₃); 0.89 (t, J = 7.3 Hz, 3H, COCH₂CH₂CH₃);
N-(5-methyl-1,3-thiazol-2-yl)-butanamide
m.p. 137-138°C

15 1H-NMR (CDCl₃) δ ppm: 11.89 (s, 1H, CONH); 7.04 (s, 1H, thiazole CH); 2.48 (t, J = 7.3 Hz, 2H, COCH₂CH₂CH₃); 2.41 (s, 3H, CH₃); 1.80 (m, 2H, COCH₂CH₂CH₃); 1.02 (t, J = 7.3 Hz, 3H, COCH₂CH₂CH₃);
N-(5-benzyl-1,3-thiazol-2-yl)-butanamide
20 m.p. 147-149°C

1H-NMR (CDCl₃) δ ppm: 7.23 (m, 5H, Ph); 7.07 (s, 1H, thiazole CH); 4.08 (s, 2H, CH₂Ph); 2.45 (t, J = 7.8 Hz, 2H, COCH₂CH₂CH₃); 1.76 (m, 2H, COCH₂CH₂CH₃); 0.97 (t, J = 7.8 Hz, 2H, COCH₂CH₂CH₃);
25 N-(5-isobutyl-1,3-thiazol-2-yl)-butanamide
m.p. 58-60°C

1H-NMR (CDCl₃) δ ppm: 7.03 (s, 1H, thiazole CH); 2.61 (d, J = 7.3 Hz, 2H, Me₂CHCH₂); 2.45 (t, J = 7.8 Hz, 2H, COCH₂CH₂CH₃); 1.81 (m, 1H, Me₂CHCH₂); 1.78 (m, 2H, COCH₂CH₂CH₃); 1.01 (t, J = 7.8 Hz, 3H, COCH₂CH₂CH₃); 0.95, 0.93 (s, 6H, Me₂CHCH₂);
N-(5-cyclopropyl-1,3-thiazol-2-yl)-butanamide;
N-{5-[2-(methylsulfonyl)ethyl]-1,3-thiazol-2-yl}-butanamide
m.p. 153-155°C

35 1H-NMR (CDCl₃) δ ppm: 11.01 (s, 1H, CONH); 7.21 (s, 1H, thiazole CH); 3.34 (m, 4H, CH₃SO₂CH₂CH₂); 2.90 (s, 3H,

CH₃SO₂); 2.48 (t, J = 7.3 Hz, 2H, COCH₂CH₂CH₃); 1.80 (m, 2H, COCH₂CH₂CH₃); 1.02 (t, J = 7.3 Hz, 3H, COCH₂CH₂CH₃); N-[5-(2-methylthioethyl)-1,3-thiazol-2-yl]-butanamide

m.p. 67-69°C

5 ¹H-NMR (CDCl₃) δ ppm: 11.63 (bs, 1H, NHCO), 7.26 (s, 1H, thiazole CH), 3.06 (t, J = 7.0 Hz, 2H, CH₃SCH₂CH₂); 2.77 (t, J = 7.0 Hz, 2H, CH₃SCH₂CH₂); 2.48 (t, J = 7.3 Hz, 2H, COCH₂CH₂CH₃); 2.14 (s, 3H, CH₃S); 1.80 (m, 2H, COCH₂CH₂CH₃); 1.02 (t, J = 7.3 Hz, 3H, COCH₂CH₂CH₃);

10 N-[5-[2-(methoxycarbonyl)ethyl]-1,3-thiazol-2-yl]-butanamide;

N-[5-(3-methoxy-propyl)-1,3-thiazol-2-yl]-butanamide

m.p. 80-82°C

1H-NMR (CDCl₃) δ ppm: 11 (sb, 1H, NHCO); 7.07 (s, 1H, H₄ thiazole); 3.41 (t, 2H, CH₂CH₂CH₂OMe); 3.34 (s 3H, OCH₃); 2.85 (t, 2H, CH₂CH₂CH₂OMe); 2.46 (t, 2H, NHCOCH₂); 1.91 (m, 2H, CH₂CH₂CH₂OMe); 1.80 (t, 2H, NHCOCH₂CH₂CH₃); 1.01 (t, 3H, NHCOCH₂CH₂CH₃);

N-[5-(2-ethoxy-ethyl)-1,3-thiazol-2-yl]-butanamide

20 m.p. 74-76°C

1H-NMR (CDCl₃) δ ppm: 7.14 (s, 1H, H₄ thiazole); 3.64 (t, 2H, CH₂CH₂OEt); 3.52 (q 2H, OCH₂CH₃); 3.02 (t, 2H, CH₂CH₂OEt); 2.47 (t, 2H, NHCOCH₂); 1.80 (m, 2H, NHCOCH₂CH₂); 1.23 (t, 3H, OCH₂CH₃); 1.02 (t, 3H, NHCOCH₂CH₂CH₃);

25 N-[5-(indol-3-yl-methyl)-1,3-thiazol-2-yl]-butanamide

m.p. 240-242°C

1H-NMR (CDCl₃) δ ppm: 9.95 (bs, 1H, CONH); 8.00 (bs, 1H, NH indole); 7.54 (d, 1H, H₄ indole); 7.36 (d, 1H, H₇ indole); 7.19 (m, 1H, H₆ indole); 7.17 (s, 1H, thiazole CH); 7.09 (m, 1H, H₅ indole); 7.07 (s, 1H, H₂ indole); 4.23 (s, 2H, CH₂); 2.39 (m 2H, CH₂CO); 1.73 (m, 2H, CH₃CH₂CH₂); 0.96 (t, 3H, CH₃CH₂CH₂).

N-[5-(3-dimethylaminoimino-buty1)-1,3-thiazol-2-yl]-butanamide.

2-amino-5-isopropyl-1,3-thiazole

2 ml (18.6 mmol) of 3-methylbutyraldehyde were dissolved in 15 ml of dioxane. 40.4 ml (18.6 mmol) of a solution 2 % v/v of bromine in dioxane was dropped therein at 0°C.

5 The mixture was maintained at room temperature under stirring for 2 hours, then 2.83 g (37.2 mmol) of thiourea and 5 ml of ethanol were added.

After 6 hours at room temperature the solution was evaporated to dryness, the residue was dissolved in 10 methylene chloride and the product extracted with 1M hydrochloric acid; the aqueous layer was made basic by using 30% ammonium hydrate and extracted again with methylene chloride. The organic phase was dried over sodium sulfate and evaporated under vacuum. The residue was 15 chromatographed on a silica gel column, eluting with cyclohexane-ethylacetate to give 1.1 g (42% yield) of the title compound.

20 $^1\text{H-NMR}$ (DMSO- d_6) δ ppm: 6.6 (s, 2H, NH₂); 6.58 (s, 1H, thiazole CH); 2.9 (m, 1H, CHMe₂); 1.18 (s, 3H, MeCHMe); 1.17 (s, 3H, MeCHMe).

Analogously the following products can be prepared starting from the suitable aldehyde:

2-amino-5-isobutyl-1,3-thiazole

25 $^1\text{H-NMR}$ (DMSO- d_6) δ ppm: 6.61 (sb, 2H, NH₂); 6.56 (s, 1H, thiazole CH); 2.39 (dd, 2H, CH₂CHMe₂); 1.65 (m, 1H, CHMe₂); 0.85 (d, 6H, CHMe₂);

2-amino-5-phenyl-1,3-thiazole;**2-amino-5-benzyl-1,3-thiazole;**

30 $^1\text{H-NMR}$ (DMSO- d_6) δ ppm: 7.3-7.2 (m, 5H, Ph); 6.68 (s, 1H, thiazole CH); 6.67 (sb, 2H, NH₂); 3.87 (s, 2H, CH₂Ph);

2-amino-5-(3-indolylmethyl)-1,3-thiazole;**2-amino-5-ethoxyethyl-1,3-thiazole;****2-amino-5-methoxypropyl-1,3-thiazole;**

35 **2-amino-5-cyclopropyl-1,3-thiazole;**

2-amino-5-methylthioethyl-1,3-thiazole;**2-amino-5-formyl-1,3-thiazole;**

2-amino-5-(3-dimethylaminoimino)butyl-1,3-thiazole.

Example 9

4-ethoxy-1-butanol

5 85 mg (0.004 mmol) of sodium were dissolved in 50 ml of methanol and 8.7 g (0.23 mol) of sodium borohydride were added. A solution of 4.6 g (0.032 mol) of methyl 4-ethoxybutanoate in 20 ml of methanol was dropped to the mixture under stirring. The reaction is maintained at reflux for 6
10 hours, then 300 ml of brine were added and the product was extracted with methylene chloride. The organic layer was dried over anhydrous sodium sulfate and evaporated to dryness to give 2.25 g (61% yield) of the title compound.

15 Analogously the following products can be prepared starting from the suitable ester:
2-cyclopropyl-1-ethanol;
3-(3-indolyl)-1-propanol; and
5-dimethylaminoimino-1-hexanol.

20

Example 10

Methyl 3-(3-indolyl)-propanoate

25 2 g (10.57 mmol) of 3-indolepropionic acid were dissolved in 50 ml of methanol. The solution was cooled to 0°C and 5 ml of sulfuric acid 96% were dropped under stirring. The solution was maintained at room temperature overnight and then poured onto ice-water, basified with 30 % ammonium hydrate and finally extracted with methylene chloride. The
30 organic layer was dried over anhydrous sodium sulfate and evaporated to dryness to give 2.3 g of an oily product (93% yield).

35 Analogously the following products can be prepared starting from the suitable carboxylic acid:

Methyl 4-ethoxy butanoate;

Methyl cyclopropylacetate; and

5-methoxycarbonylethyl-2-amino-1,3-thiazole.

Example 11**4-methyl-pentanal**

1.24 ml (14.18 mmol) of oxalyl chloride were dissolved in
5 10 ml of methylene chloride and after cooling to -60°C,
2.31 ml of DMSO (35 mmoles) were dropped.

After 5 minutes at the same temperature, a solution of 1 ml
(11.9 mmol) of 4-methyl-1-pentanol in 10 ml of methylene
chloride was slowly dropped. The mixture was maintained
10 under stirring for 30 minutes at the same temperature, then
8.3 ml (59.5 mmol) of triethylamine were added. After 2
hours at 0°C water was added. The mixture was diluted with
methylene chloride and washed successively with 1M
15 hydrochloric acid, water, saturated sodium bicarbonate and
finally with brine. The organic layer was dried over
anhydrous sodium sulfate and evaporated to dryness to give
0.7 g (25% yield) of the title compound.

Analogously the following products can be prepared starting
from the suitable alcohol:

20 2-cyclopropyl-1-ethanal;
4-methylthio-1-butanal;
4-ethoxy-1-butanal;
5-methoxy-1-pentanal; and
5-dimethylaminoimino-1-hexanal.

25

Example 12**5-benzyloxy-1-methoxy-pentane**

1.6 g (0.039 mol) of 55% sodium hydride in oil were added to
50 ml of dimethylformamide under stirring at room
30 temperature. 5 ml (0.026 mol) of 5-benzyloxy-1-pentanol and
2.43 ml (0.039 mol) of methyl iodide were then added
successively. After a night the excess of sodium hydride
was decomposed with water and the solvent evaporated under
vacuum. The residue was redissolved with methylene
35 chloride and washed with water. The organic layer was
finally dried over anhydrous sodium sulfate and evaporated
to give 3.5 g (70% yield) of the title compound.

Analogously, by using ethyl iodide, the following compound can be prepared:

4-ethoxy-butanoic acid.

5 **Example 13**

5-methoxy-1-pentanol

3.5 g (0.018 mol) of 5-benzyloxy-1-methoxy-pentane were dissolved in 50 ml of ethanol and 400 mg of 10% palladium on activated charcoal were added. The mixture was 10 hydrogenated at 40 psi at room temperature for 5 hours, then filtered on celite and evaporated under vacuum to give 1.77 g (84% yield) of the title compound.

Example 14

15 **Ethyl 5-dimethylaminoimino-hexanoate**

15.8 g (100 mmol) of ethyl 4-acetyl-butanoate and 6 g (100 mmol) of anhydrous N,N-dimethyl hydrazine in 50 ml of toluene containing 0.1 ml of trifluoroacetic acid were heated at 70 °C for 5 hours. The mixture was then washed 20 with water, dried over anhydrous sodium sulfate and evaporated to give 12.3 g (79% yield) of the title compound.

Example 15

25 **N-[5-(3-oxo-butyl)-1,3-thiazol-2-yl]-butanamide**

To a stirred solution of 200 mg (1 mmol) of cupric acetate in 10 ml of water 141 mg (0.5 mmol) of N-[5-(3-dimethylaminoimino-butyl)-1,3-thiazol-2-yl]-butanamide in 10 ml of tetrahydrofuran were added. After 2 hours the 30 solvent was removed under reduced pressure, a mixture of aqueous ammonium chloride and ammonium hydroxide was added and the product extracted with methylene chloride to give after drying and concentration 114 mg (95% yield) of the title compound.

35

Example 16

2-benzyloxycarbonylamino-5-formyl-1,3-thiazole

1 g (7.8 mmol) of 2-amino-5-formyl-1,3-thiazole was dissolved in 25 ml of tetrahydrofuran and 1.35 ml (9.36 mmol) of triethylamine and 1.33 ml (9.36 mmol) of benzylchloroformate were added at 0°C under stirring. After 5 8 hours at room temperature the solvent was evaporated, the residue redissolved with methylene chloride and washed with saturated tartaric acid and then with water. The solvent was dried over anhydrous sodium sulfate and evaporated. The residue was purified by chromatography on silica gel using 10 cyclohexane-ethylacetate as eluent to give 1.3 g (65% yield) of the title compound.

Example 17**5-hydroxymethyl-2-benzyloxycarbonylamino-1,3-thiazole**

15 530 mg (14 mmol) of sodium borohydride were added in small portions to a stirred solution of 7 g (27 mmol) of 2-benzyloxycarbonylamino-5-formyl-1,3-thiazole in 80 ml of methanol at room temperature. The reaction went on for 2 hours. After evaporation of the solvent the residue was 20 purified by chromatography (cyclohexane-ethylacetate) to give 5.05 g (71% yield) of the title compound.

Example 18**2-benzyloxycarbonylamino-5-(4-phenyl-1-sulfonyloxy)methyl-1,3-thiazole**

25 To a solution of 1 g (3.78 mmol) of 2-benzyloxycarbonylamino-5-hydroxymethyl-1,3-thiazole in 25 ml of pyridine 0.86 g (4.54 mmol) of tosyl chloride in 10 ml of pyridine were dropped at 0°C. After stirring at room 30 temperature for 6 hours the solvent was evaporated under vacuum, the residue redissolved with methylene chloride, washed with 1M hydrochloric acid and finally with water. The organic layer was dried over anhydrous sodium sulfate and evaporated. The residue was purified by chromatography 35 on silica gel (cyclohexane-ethylacetate) to give 1.2 g (80% yield) of the title compound.

Example 19

2-benzyloxycarbonylamino-5-(2-ethoxycarbonyl-3-ethoxycarbonylethyl)-1,3-thiazole

To a suspension of 321 mg of 55% sodium hydride in oil (7.4 mmol) in 20 ml of tetrahydrofuran 1.12 ml (7.4 mmol) of 5 diethylmalonate were added. After 30 minutes, a solution of 1.5 g (3.7 mmol) of 2-benzyloxycarbonylamino-5-(4-phenyl-1-sulphonyloxy)methyl-1,3-thiazole in 10 ml of the same solvent was dropped under stirring. After 6 hours the solvent was evaporated and the residue redissolved with 10 methylene chloride and washed with water. The organic layer was dried over anhydrous sodium sulfate and evaporated. The residue was chromatographed on a silica gel column (cyclohexane-ethylacetate) to give 1.05 g (70% yield) of the title compound.

15

Example 20

2-benzyloxycarbonylamino-5-ethoxycarbonylethyl-1,3-thiazole

To a solution of 4.06 g (10 mmol) of 2-benzyloxycarbonylamino-5-(2-ethoxycarbonyl-3-ethoxycarbonylethyl)-1,3-thiazole in 10 ml of 20 dimethylsulphoxide 0.64 g (11 mmol) of sodium chloride and 0.36 (20 mmol) of water were added under stirring. The mixture was heated at 160 °C for 8 hours and then the solvent removed under vacuum. The residue was redissolved 25 with methylene chloride and washed with brine. After drying and concentration the residue was chromatographed on a silica gel column (cyclohexane-ethylacetate) to give 2.67 g (80% yield) of the title compound.

30 **Example 21**

2-amino-5-carboxyethyl-1,3-thiazole

1 g (2.9 mmol) of 2-benzyloxycarbonylamino-5-ethoxycarbonylethyl-1,3-thiazole was dissolved in 20 ml of 33% hydrobromic acid in acetic acid. After 2 hours at room 35 temperature, the solvent was evaporated under vacuum. The residue was redissolved in the minimum amount of water and the hydrobromide of the title compound was precipitated by adding diethylether (75% yield).

Example 22**Preparation of methyl 2-[3-(3-chloropropoxy)phenyl]acetate**

A mixture of methyl (m-hydroxyphenyl)acetate ((5 g, 0.03 moles), 1-bromo-3-chloropropane (3.26 ml, 0.03 moles) and anhydrous potassium carbonate (6.4 g) in anhydrous acetone (60 ml) was refluxed for 40 hours. After cooling, the precipitate was filtered off and the solution was evaporated to dryness to give the product as an oil, which 10 was purified by flash chromatography with hexane:AcOEt (97:3) as eluent (6.2 g, 85% yield).

Analogously, the following product can be prepared:

methyl 2-[3-(2-chloroethoxy)phenyl]acetate.

15 Example 23**Preparation of 2-[3-(3-chloropropoxy)phenyl]acetic acid**

A mixture of methyl 2-[3-(3-chloropropoxy)phenyl]acetate (4.95 g, 0.02 moles) and a solution of 1N sodium hydroxide (0.02 moles) was stirred at room temperature for 24 hours.

20 After acidification the acid separated as white powder (4.53 g, 97% yield)

m.p. 83-84°C

Analogously, the following product can be prepared:

2-[3-(2-chloroethoxy)phenyl]acetic acid

25 m.p. 100-101°C.

Example 24**Preparation of N-(5-isopropyl-1,3-thiazol-2-yl)-2-[3-[3-(4-morpholinyl)propoxy]phenyl]acetamide**

30 A mixture of 2-[3-(3-chloropropoxy)phenyl]-N-(5-isopropyl-1,3-thiazol-2-yl)acetamide (1.00 g, 2.8 mmoles), morpholine (1.24 ml, 14.2 mmoles), potassium iodide (0.24 g, 1.4 mmoles) in anhydrous dimethylformamide (3.5 ml) was heated at 100°C for 6 hours. The solution was acidified and extracted with ether to eliminate unreacted products; then 35 the solution was basified and extracted with ether. The solvent was evaporated to dryness to give the product as an oily semisolid which was purified by flash chromatography

with dichloromethane:methanol (97:3) as eluent (1.0 g, 87% yield)

¹H-NMR (DMSO-d₆) δ ppm: 12.09 (bs, 1H, CONH); 7.21 (t, 1H, H5 Ph); 7.13 (s, 1H, thiazole CH); 6.8-6.9 (m, 3H, H2, H4, H6 Ph); 3.97 (t, 2H, OCH₂CH₂CH₂N); 3.66 (s, 2H, COCH₂); 3.54 (t, 2H, OCH₂CH₂N); 3.07 (ept, 1H, CHMe₂); 2.39 (t, 2H, OCH₂CH₂CH₂N); 2.33 (t, 2H, OCH₂CH₂N); 2.14 (quint, 2H, OCH₂CH₂CH₂N); 1.22 (d, 6H, CHMe₂).

10 Analogously, the following product can be prepared:

N-(5-isopropyl-1,3-thiazol-2-yl)-2-{3-[2-(4-morpholinyl)ethoxy]phenyl}acetamide

¹H-NMR (DMSO-d₆) δ ppm: 12.11 (bs, 1H, CONH); 7.20 (t, 1H, H5 Ph); 7.13 (d, 1H, thiazole CH); 6.7-6.9 (m, 3H, H2, H4, H6 Ph); 4.04 (t, 2H, OCH₂CH₂N); 3.66 (s, 2H, COCH₂); 3.55 (m, 4H, OCH₂CH₂N morpholine); 3.08 (m, 1H, CHMe₂); 2.66 (t, 2H, OCH₂CH₂N); 2.44 (m, 4H, OCH₂CH₂N morpholine); 1.22 (d, 6H, CHMe₂);

20 N-(5-isopropyl-1,3-thiazol-2-yl)-2-{3-[3-(1-pyrrolidinyl)propoxy]phenyl}acetamide

¹H-NMR (DMSO-d₆) δ ppm: 12.1 (bs, 1H, CONH); 7.19 (t, 1H, H5 Ph); 7.13 (d, 1H, thiazole CH); 6.7-6.9 (m, 3H, H2, H4, H6 Ph); 3.97 (t, 2H, OCH₂CH₂CH₂N); 3.66 (s, 2H, COCH₂); 3.08 (m, 1H, CHMe₂); 2.50 (m, 2H, OCH₂CH₂CH₂N); 2.41 (m, 4H, CH₂N 25 pirrolidine); 1.85 (m, 2H, OCH₂CH₂CH₂N); 1.65 (m, 4H, CH₂CH₂N pirrolidine); 1.23 (d, 6H, CHMe₂);

N-(5-isopropyl-1,3-thiazol-2-yl)-2-{3-[3-(4-methyl-1-piperazinyl)propoxy]phenyl}acetamide

¹H-NMR (DMSO-d₆) δ ppm: 12.1 (bs, 1H, CONH); 7.19 (t, 1H, H5 Ph); 7.13 (d, 1H, thiazole CH); 6.7-6.9 (m, 3H, H2, H4, H6 Ph); 3.95 (t, 2H, OCH₂CH₂CH₂N); 3.66 (s, 2H, COCH₂); 3.08 (m, 1H, CHMe₂); 2.15-2.45 (m, 10H, OCH₂CH₂CH₂N+piperazine); 2.11 (s, 3H, NMe); 1.82 (m, 2H, OCH₂CH₂CH₂N); 1.22 (d, 6H, CHMe₂).

35 2-{3-[2-(dimethylamino)ethoxy]phenyl}-N-(5-isopropyl-1,3-thiazol-2-yl)acetamide

¹H-NMR (DMSO-d₆) δ ppm: 12.08 (bs, 1H, CONH); 7.2-6.90 (m,

5H, Ph+thiazole CH); 4.00 (t, 2H, OCH₂CH₂N); 3.66 (s, 2H, COCH₂); 3.07 (m, 1H, CHMe₂); 2.59 (t, 2H, OCH₂CH₂N); 2.11 (s, 3H, NMe); 2.19 (s, 6H, Me₂N); 1.22 (d, 6H, CHMe₂); 2-{3-[3-(dimethylamino)propoxy]phenyl}-N-(5-isopropyl-1,3-thiazol-2-yl)acetamide
10 ¹H-NMR (DMSO-d₆) δ ppm: 12.05 (bs, 1H, CONH); 7.19-6.79 (m, 5H, Ph+thiazole CH); 3.95 (t, 2H, OCH₂CH₂CH₂N); 3.66 (s, 2H, COCH₂); 3.08 (m, 1H, CHMe₂); 2.32 (t, 2H, OCH₂CH₂CH₂N); 2.11 (s, 3H, NMe₂); 1.81 (m, 2H, OCH₂CH₂CH₂N); 1.22 (d, 6H, CHMe₂). | |

Example 25**Preparation of 2-[N-[2'-N'-(ethoxycarbonyl-methyl)-aminol-acetyl]-amino-5-bromo-thiazole**

15 A solution of N-(5-bromo-1,3-thiazol-2-yl)-2-bromoacetamide (0.35 g, 1.17 mmol) in DMF (5 ml) was added dropwise to a solution of glycine ethyl ester hydrochloride (0.33 g, 2.33 mmol) and triethylamine (0.49 ml, 3.5 mmol) in DMF (10 ml). After 3 hours at room temperature, the reaction mixture was
20 heated at 40°C for about 5 hours and then diluted with water and extracted with methylene chloride. The combined organic layers were washed with brine, dried, concentrated and chromatographed on silica gel using cyclohexane:ethyl acetate 7:3 as eluent. The title compound was obtained as a
25 colourless solid (0.15 g, 43%)

m.p. 115-116°C

¹H-NMR (DMSO-d⁶) δ ppm: 7.46 (s, 1H, H₄thiaz), 4.05 (q, 2H, OCH₂CH₃), 3.49 (s, 2H, NHCOCH₂), 3.4 (s, 2H, NHCH₂), 1.18 (t, 3H, OCH₂CH₃). |

30

Analogously, the following compound can be prepared:

2-anilino-N-(5-isopropyl-1,3-thiazol-2-yl)acetamide: m.p.
143-145°C

¹H-NMR (DMSO-d⁶) δ ppm: 11.92 (s, 1H, NHCO), 7.13 (s, 1H, H₄thiaz), 7.06-6.6 (m, 5H, Ph), 6.0 (t, 1H, NHCH₂), 3.95 (d, 2H, NHCH₂), 3.08 (m, 1H, CHMe₂), 1.23 (d, 6H, CHMe₂). |

Example 26**Preparation of N-(5-isopropyl-1,3-thiazol-2-yl)-2-(2-bromophenyl)acetamide**

5 To a suspension of resin N-Cyclohexylcarbodiimide N'-methylpolystyrene (0.251 g, 2.39 mmol g⁻¹, 0.6 mmol), previously washed with DCM (3X5 ml), in DCM (4 ml) at room temperature, 2-bromophenylacetic acid (0.086 g, 0.4 mmol) was added. After 10 min., a solution of 2-amino-5-isopropyl-1,3-thiazole (0.0284 g, 0.2 mmol) in DCM (4 ml) was added. The mixture was shaked for 24 hours at room temperature, the resin filtered and washed with DCM (3X10 ml). The filtrated were combined, washed with water, 5% HCl, water, saturated sodium bicarbonate and water, dried 15 over sodium sulfate and evaporated.

¹H-NMR (DMSO-d⁶) δ ppm: 10.05 (s broad, 1H, NHCOCH₂), 7.6-7.2 (m, 4H, Ar), 7.08 (s, 1H, H4thiaz), 3.98 (s, 2H, NHCOCH₂), 3.11 (m, 1H, CHMe₂), 1.31 (d, 6H, CHMe₂)

20 All the compounds were characterised by Mass Spectroscopy (MS). LC-MS confirmed that in each case the principle component had a molecular ion corresponding to the expected product.

25 Chromatography: Reverse phase HPLC with UV detection were run.

Mobile A: water (0.1% TFA)

Mobile B: acetonitrile:water 95:5 (0.1% TFA)

Flow rate: 1ml/min

30 Gradient: 10-100% B in 12 minutes, hold 100% B 3 min, return 10% B in 5 min

Detection: UV monitor 215, 254 and 300 nm

Sample were prepared as dilute solutions in acetonitrile (1-1.5 mM).

35 The compounds showed an HPLC area % ranging from 40 to 100%.

Starting from the suitable carboxylic acid, the following compounds can be prepared:

N-(5-isopropyl-1,3-thiazol-2-yl)-2-(2,3,4,5,6-
5 pentafluorophenyl)acetamide;

N-(5-isopropyl-1,3-thiazol-2-yl)-2-(2-
chlorophenyl)acetamide;

N-(5-isopropyl-1,3-thiazol-2-yl)-2-(2-
nitrophenyl)acetamide;

10 N-(5-isopropyl-1,3-thiazol-2-yl)-2-(2-
trifluoromethylphenyl)acetamide;

N-(5-isopropyl-1,3-thiazol-2-yl)-2-(2-
methoxyphenyl)acetamide;

N-(5-isopropyl-1,3-thiazol-2-yl)-2-(2,5-
15 dimethoxyphenyl)acetamide;

N-(5-isopropyl-1,3-thiazol-2-yl)-2-(2,5-
difluorophenyl)acetamide;

N-(5-isopropyl-1,3-thiazol-2-yl)-2-(3,4,5-
trimethoxyphenyl)acetamide;

20 N-(5-isopropyl-1,3-thiazol-2-yl)-2-(2,6-
dichlorophenyl)acetamide;

N-(5-isopropyl-1,3-thiazol-2-yl)-2-(2-chloro-6-
fluorophenyl)acetamide;

N-(5-isopropyl-1,3-thiazol-2-yl)-2-(3,5-
25 dimethoxyphenyl)acetamide;

N-(5-isopropyl-1,3-thiazol-2-yl)-2-(3,5-
difluorophenyl)acetamide;

N-(5-isopropyl-1,3-thiazol-2-yl)-2-(2,5-bis-
trifluoromethylphenyl)acetamide;

30 N-(5-isopropyl-1,3-thiazol-2-yl)-2-(4-
methylthiophenyl)acetamide;

N-(5-isopropyl-1,3-thiazol-2-yl)-2-(4-
methoxyphenyl)acetamide;

N-(5-isopropyl-1,3-thiazol-2-yl)-2-(4-
35 bromophenyl)acetamide;

N-(5-isopropyl-1,3-thiazol-2-yl)-2-(4-
chlorophenyl)acetamide;

N-(5-isopropyl-1,3-thiazol-2-yl)-2-(4-nitrophenyl)acetamide;

N-(5-isopropyl-1,3-thiazol-2-yl)-2-(4-trifluoromethylphenyl)acetamide;

5 N-(5-isopropyl-1,3-thiazol-2-yl)-2-(4-methylphenyl)acetamide;

N-(5-isopropyl-1,3-thiazol-2-yl)-2-(3-trifluoromethylphenyl)acetamide;

N-(5-isopropyl-1,3-thiazol-2-yl)-2-(3-10 chlorophenyl)acetamide;

N-(5-isopropyl-1,3-thiazol-2-yl)-2-(3-methoxyphenyl)acetamide;

N-(5-isopropyl-1,3-thiazol-2-yl)-2-(2,4-dinitrophenyl)acetamide;

15 N-(5-isopropyl-1,3-thiazol-2-yl)-2-(2,4-dichlorophenyl)acetamide;

N-(5-isopropyl-1,3-thiazol-2-yl)-2-(2,4-difluorophenyl)acetamide;

N-(5-isopropyl-1,3-thiazol-2-yl)-2-(4-benzyloxy-3-20 methoxyphenyl)acetamide;

N-(5-isopropyl-1,3-thiazol-2-yl)-2-(3,4-dichlorophenyl)acetamide;

N-(5-isopropyl-1,3-thiazol-2-yl)-2-(3,4-difluorophenyl)acetamide;

25 2-cyclopentyl-N-(5-isopropyl-1,3-thiazol-2-yl)-2-phenylacetamide;

2-cyclohexyl-N-(5-isopropyl-1,3-thiazol-2-yl)-2-phenylacetamide;

N-(5-isopropyl-1,3-thiazol-2-yl)-2,2-diphenylacetamide;

30 N-(5-isopropyl-1,3-thiazol-2-yl)-2-(2-nitrophenoxy)acetamide;

N-(5-isopropyl-1,3-thiazol-2-yl)-2-(4-nitrophenyl)propanamide;

N-(5-isopropyl-1,3-thiazol-2-yl)-2-(4-35 isobutylphenyl)propanamide;

N-(5-isopropyl-1,3-thiazol-2-yl)-2-oxo-2-phenylacetamide;

N-(5-isopropyl-1,3-thiazol-2-yl)-3-methyl-2-phenylpentanamide;

(E, Z)-N-(5-isopropyl-1,3-thiazol-2-yl)-2-phenyl-2-butenamide;

N-(5-isopropyl-1,3-thiazol-2-yl)bicyclo[4.2.0]octa-1,3,5-triene-7-carboxamide;

5 N-(5-isopropyl-1,3-thiazol-2-yl)-2-phenylbutanamide;

tert-butyl (1R)-2-[(5-isopropyl-1,3-thiazol-2-yl)amino]-2-oxo-1-phenylethylcarbamate;

(1R)-2-[(5-isopropyl-1,3-thiazol-2-yl)amino]-2-oxo-1-phenylethyl acetate;

10 (1S)-2-[(5-isopropyl-1,3-thiazol-2-yl)amino]-2-oxo-1-phenylethyl acetate;

2-(acetylamino)-N-(5-isopropyl-1,3-thiazol-2-yl)-2-phenylacetamide;

(R)-2-(methoxy)-N-(5-isopropyl-1,3-thiazol-2-yl)-2-phenylacetamide;

15 3,3,3-trifluoro-N-(5-isopropyl-1,3-thiazol-2-yl)-2-methoxy-2-phenylpropanamide;

2-(2,4-dinitrophenyl)-N-(5-isopropyl-1,3-thiazol-2-yl)acetamide;

20 N-(5-isopropyl-1,3-thiazol-2-yl)-2-(5-benzyloxy-1H-indol-3-yl)acetamide;

N-(5-isopropyl-1,3-thiazol-2-yl)-2-(3-methoxy-2-methyl-1H-indol-3-yl)acetamide;

2-(1H-indol-3-yl)-N-(5-isopropyl-1,3-thiazol-2-yl)-2-

25 oxoacetamide;

2-[1-(4-chlorobenzoyl)-5-methoxy-2-methyl-1H-indol-3-yl]-N-(5-isopropyl-1,3-thiazol-2-yl)acetamide;

4-(1H-indol-3-yl)-N-(5-isopropyl-1,3-thiazol-2-yl)butanamide;

30 N-(5-isopropyl-1,3-thiazol-2-yl)-3-(2-thienyl)propanamide

2-(5-chloro-1-benzothiophen-3-yl)-N-(5-isopropyl-1,3-thiazol-2-yl)acetamide;

2-(1-benzothiophen-3-yl)-N-(5-isopropyl-1,3-thiazol-2-yl)acetamide;

35 2-[2-(formylamino)-1,3-thiazol-4-yl]-N-(5-isopropyl-1,3-thiazol-2-yl)-2-(methoxyimino)acetamide;

2-{2-[(2-chloroacetyl)amino]-1,3-thiazol-4-yl}-N-(5-isopropyl-1,3-thiazol-2-yl)-2-(methoxyimino)acetamide;

2-chloro-N-(4-{2-[(5-isopropyl-1,3-thiazol-2-yl)amino]-2-oxoethyl}-1,3-thiazol-2-yl)acetamide;
ethyl 2-({[2-[(5-isopropyl-1,3-thiazol-2-yl)amino]-2-oxo-1-(1H-pyrazol-3-yl)ethylidene]amino}oxy)acetate;

5 N-(5-isopropyl-1,3-thiazol-2-yl)-4-oxo-4-(4-methylphenyl)butanamide;
N-(5-isopropyl-1,3-thiazol-2-yl)-4-(4-nitrophenyl)butanamide;
N-(5-isopropyl-1,3-thiazol-2-yl)-4-phenylbutanamide;

10 benzyl 4-[(5-isopropyl-1,3-thiazol-2-yl)amino]-4-oxobutylcarbamate;
4-(1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl)-N-(5-isopropyl-1,3-thiazol-2-yl)butanamide;
N-(5-isopropyl-1,3-thiazol-2-yl)-4-(4-methoxy-1-naphthyl)-

15 4-oxobutanamide;
3-(2-chlorophenoxy)-N-(5-isopropyl-1,3-thiazol-2-yl)propanamide;
3-(4-methylphenoxy)-N-(5-isopropyl-1,3-thiazol-2-yl)propanamide;

20 3-cyclopentyl-N-(5-isopropyl-1,3-thiazol-2-yl)propanamide;
3-cyclohexyl-N-(5-isopropyl-1,3-thiazol-2-yl)propanamide;
N-(5-isopropyl-1,3-thiazol-2-yl)-4-methylpentanamide;
3-(4-chlorophenyl)-N-(5-isopropyl-1,3-thiazol-2-yl)propanamide;

25 3-(4-methoxyphenyl)-N-(5-isopropyl-1,3-thiazol-2-yl)propanamide; | |
3-chloro-N-(5-isopropyl-1,3-thiazol-2-yl)propanamide; | |
3-phenyl-N-(5-isopropyl-1,3-thiazol-2-yl)propanamide; | |
N-(5-isopropyl-1,3-thiazol-2-yl)-5-oxo-5-phenylpentanamide;

30 2-[(5-isopropyl-1,3-thiazol-2-yl)amino]-2-oxo-1-phenylethyl acetate;
N-(5-isopropyl-1,3-thiazol-2-yl)-2-[4-(1-oxo-1,3-dihydro-2H-isoindol-2-yl)phenyl]propanamide;

35 1-(4-chlorophenyl)-N-(5-isopropyl-1,3-thiazol-2-yl)cyclopentanecarboxamide;
1-phenyl-N-(5-isopropyl-1,3-thiazol-2-yl)cyclopentanecarboxamide;

2-(3-bromo-4-methoxyphenyl)-N-(5-isopropyl-1,3-thiazol-2-yl)acetamide;
2-(2-nitro-4-trifluoromethylphenyl)-N-(5-isopropyl-1,3-thiazol-2-yl)acetamide;
5 5-cyclohexyl 1-(4-{2-[(5-isopropyl-1,3-thiazol-2-yl)amino]-2-oxoethyl}benzyl) (2S)-2-[(tert-butoxycarbonyl)amino]pentanedioate;
2-(5,6-dimethyl-1H-benzimidazol-1-yl)-N-(5-isopropyl-1,3-thiazol-2-yl)acetamide;
10 2-[5-(4-chlorophenyl)-2H-1,2,3,4-tetraazol-2-yl]-N-(5-isopropyl-1,3-thiazol-2-yl)acetamide;
N-(5-isopropyl-1,3-thiazol-2-yl)-2-[5-(1-pyrrolidinyl)-2H-1,2,3,4-tetraazol-2-yl]acetamide;
N-(5-isopropyl-1,3-thiazol-2-yl)-2-(3-methyl-1-benzothiophen-2-yl)acetamide;
15 N-(5-isopropyl-1,3-thiazol-2-yl)-4,4-bis(4-methylphenyl)-3-butenamide;
2-cyclopropyl-N-(5-isopropyl-1,3-thiazol-2-yl)acetamide;
N-{4-bromo-6-[(5-isopropyl-1,3-thiazol-2-yl)amino]-6-
20 oxohexyl}benzamide;
2-cyclopentyl-N-(5-isopropyl-1,3-thiazol-2-yl)acetamide;
benzyl 6-[(5-isopropyl-1,3-thiazol-2-yl)amino]-6-oxohexylcarbamate;
N~1~~(5-isopropyl-1,3-thiazol-2-yl)-N~4~~(2-propynyl)-2-
25 butenediamide; |
4-(2,4-dimethylphenyl)-N-(5-isopropyl-1,3-thiazol-2-yl)-4-oxobutanamide; |
4-(4-benzyloxyphenyl)-N-(5-isopropyl-1,3-thiazol-2-yl)-4-oxobutanamide; |
30 4-(thiphen-2-yl)-N-(5-isopropyl-1,3-thiazol-2-yl)-4-oxobutanamide;
benzyl 2-[(benzyloxy)carbonyl]amino]-5-[(5-isopropyl-1,3-thiazol-2-yl)amino]-5-oxopentanoate;
4-(1H-indol-3-yl)-N-{3-[(5-isopropyl-1,3-thiazol-2-
35 yl)amino]-3-oxopropyl}butanamide;
4-[(5-isopropyl-1,3-thiazol-2-yl)amino]carbonylphenyl 4-chlorobenzenesulfonate;

WO 00/26202

-67-

N-(5-isopropyl-1,3-thiazol-2-yl)-4-[(2-methoxyanilino)carbonyl]amino)benzamide;
 4-[(2-(isopropylsulfonyl)acetyl)amino)-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide;
 5 N-(5-isopropyl-1,3-thiazol-2-yl)-4-[(2-(phenylsulfamido)acetyl)amino)-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide;
 4-[(diethylamino)sulfonyl]-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide;
 2-bromo-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide;
 10 3,5-difluoro-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide;
 3-[(2-fluoroanilino)carbonyl]amino)-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide;
 N-(5-isopropyl-1,3-thiazol-2-yl)-1-phenyl-5-propyl-1H-pyrazole-4-carboxamide;
 15 3-chloro-4-(methylsulfamido)-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide;
 2-[(4-chlorophenyl)sulfonyl]-N-(5-isopropyl-1,3-thiazol-2-yl)-2-thiophenecarboxamide;
 3-iodo-4-(methylsulfamido)-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide;
 20 5-(4-chlorophenyl)-N-(5-isopropyl-1,3-thiazol-2-yl)-2-thiophenecarboxamide;
 3,5-dichloro-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide;
 3,4-dichloro-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide;
 2,4-dichloro-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide;
 25 3-iodio-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide;
 2-iodio-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide;
 4-iodio-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide;
 30 3-bromo-2-fluoro-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide;
 4-chloro-2-fluoro-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide;
 5-bromo-2-chloro-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide;
 3-chloro-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide;
 2-chloro-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide;
 35 2-fluoro-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide;
 2-fluoro-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide;
 2,4-difluoro-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide;

WO 00/26202

- 68 -

3,4-difluoro-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide;
2,3,4,5,6-pentafluoro-N-(5-isopropyl-1,3-thiazol-2-
y1)benzamide;
N-(5-isopropyl-1,3-thiazol-2-yl)-4-methyl-3-nitrobenzamide;
N-(5-isopropyl-1,3-thiazol-2-yl)-5-methyl-2-nitrobenzamide;
N-(5-isopropyl-1,3-thiazol-2-yl)-3-methyl-2-nitrobenzamide;
N-(5-isopropyl-1,3-thiazol-2-yl)-3,5-dimethyl-4-
nitrobenzamide;
N-(5-isopropyl-1,3-thiazol-2-yl)-4-methoxy-2-
nitrobenzamide;
N-(5-isopropyl-1,3-thiazol-2-yl)-3-methoxy-2-
nitrobenzamide;
N-(5-isopropyl-1,3-thiazol-2-yl)-4-methoxy-3-
nitrobenzamide;
N-(5-isopropyl-1,3-thiazol-2-yl)-3,5-dinitrobenzamide;
5-[(5-isopropyl-1,3-thiazol-2-yl)-3-methoxy-4-
nitrophenyl octanoate;
N-(5-isopropyl-1,3-thiazol-2-yl)-2-nitrobenzamide;
4-chloro-N-(5-isopropyl-1,3-thiazol-2-yl)-4-nitrobenzamide;
4-chloro-N-(5-isopropyl-1,3-thiazol-2-yl)-3-nitrobenzamide;
2-chloro-N-(5-isopropyl-1,3-thiazol-2-yl)-2-nitrobenzamide;
5-chloro-N-(5-isopropyl-1,3-thiazol-2-yl)-4-nitrobenzamide;
2-bromo-N-(5-isopropyl-1,3-thiazol-2-yl)-5-nitrobenzamide;
4-fluoro-N-(5-isopropyl-1,3-thiazol-2-yl)-3-nitrobenzamide;
4-fluoro-N-(5-isopropyl-1,3-thiazol-2-yl)-2-nitrobenzamide;
N-(5-isopropyl-1,3-thiazol-2-yl)-3,5-
(trifluoromethyl)benzamide;
N-(5-isopropyl-1,3-thiazol-2-yl)-3,5-
bis(trifluoromethyl)benzamide;
N-(5-isopropyl-1,3-thiazol-2-yl)-2,6-
bis(trifluoromethyl)benzamide;
N-(5-isopropyl-1,3-thiazol-2-yl)-2-
(trifluoromethyl)benzamide;
N-(5-isopropyl-1,3-thiazol-2-yl)-3-
(trifluoromethyl)benzamide;

3-fluoro-N-(5-isopropyl-1,3-thiazol-2-yl)-4-
(trifluoromethyl)benzamide;
2-fluoro-N-(5-isopropyl-1,3-thiazol-2-yl)-3-
(trifluoromethyl)benzamide;
5 5-fluoro-N-(5-isopropyl-1,3-thiazol-2-yl)-3-
(trifluoromethyl)benzamide;
2-fluoro-N-(5-isopropyl-1,3-thiazol-2-yl)-4-
(trifluoromethyl)benzamide;
4-fluoro-N-(5-isopropyl-1,3-thiazol-2-yl)-3-
10 (trifluoromethyl)benzamide;
methyl 2-[(5-isopropyl-1,3-thiazol-2-
y1)amino]carbonyl}benzoate;
4-cyano-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide;
3-cyano-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide;
15 N-(5-isopropyl-1,3-thiazol-2-yl)-3-methylbenzamide;
N-(5-isopropyl-1,3-thiazol-2-yl)-2-methylbenzamide;
N-(5-isopropyl-1,3-thiazol-2-yl)-4-methylbenzamide;
N-(5-isopropyl-1,3-thiazol-2-yl)-4-vinylbenzamide;
N-(5-isopropyl-1,3-thiazol-2-yl)-4-(2-
20 phenylethynyl)benzamide;
N-(5-isopropyl-1,3-thiazol-2-yl)-3-methoxy-4-
methylbenzamide;
2-benzyl-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide;
N-(5-isopropyl-1,3-thiazol-2-yl)-2-phenethylbenzamide;
25 N-(5-isopropyl-1,3-thiazol-2-yl)-2-phenylbenzamide;
N-(5-isopropyl-1,3-thiazol-2-yl)-4-phenylbenzamide;
4-(tert-butyl)-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide;
N-(5-isopropyl-1,3-thiazol-2-yl)-4-isopropylbenzamide;
N-(5-isopropyl-1,3-thiazol-2-yl)-4-pentylbenzamide;
30 3-fluoro-N-(5-isopropyl-1,3-thiazol-2-yl)-4-
methylbenzamide;
N-(5-isopropyl-1,3-thiazol-2-yl)-3,4-dimethylbenzamide;
N-(5-isopropyl-1,3-thiazol-2-yl)-3,5-dimethylbenzamide;
N-(5-isopropyl-1,3-thiazol-2-yl)-4-
35 (methylsulfonyl)benzamide;
3-fluoro-N-(5-isopropyl-1,3-thiazol-2-yl)-4-
methoxybenzamide;

3-chloro-N-(5-isopropyl-1,3-thiazol-2-yl)-4-methoxybenzamide;

5-chloro-N-(5-isopropyl-1,3-thiazol-2-yl)-2-methoxybenzamide;

5 N-(5-isopropyl-1,3-thiazol-2-yl)-4-methoxybenzamide;

N-(5-isopropyl-1,3-thiazol-2-yl)-3-methoxybenzamide;

N-(5-isopropyl-1,3-thiazol-2-yl)-2-methoxybenzamide;

N-(5-isopropyl-1,3-thiazol-2-yl)-3,4-dimethoxybenzamide;

N-(5-isopropyl-1,3-thiazol-2-yl)-3,5-dimethoxybenzamide;

10 N-(5-isopropyl-1,3-thiazol-2-yl)-2,4-dimethoxybenzamide;

N-(5-isopropyl-1,3-thiazol-2-yl)-2,3-dimethoxybenzamide;

N-(5-isopropyl-1,3-thiazol-2-yl)-3-phenoxybenzamide;

N-(5-isopropyl-1,3-thiazol-2-yl)-2-phenoxybenzamide;

N-(5-isopropyl-1,3-thiazol-2-yl)-4-phenoxybenzamide;

15 2-ethoxy-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide;

4-ethoxy-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide;

N-(5-isopropyl-1,3-thiazol-2-yl)-3,4,5-trimethoxybenzamide;

3,4-diethoxy-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide;

3,4,5-triethoxy-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide

20 N-(5-isopropyl-1,3-thiazol-2-yl)-3-methoxy-4-(methoxymethoxy)benzamide;

4-butoxy-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide;

N-(5-isopropyl-1,3-thiazol-2-yl)-4-propoxybenzamide;

4-isopropoxy-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide;

25 N-(5-isopropyl-1,3-thiazol-2-yl)-1,3-benzodioxole-5-carboxamide;

4-(benzyloxy)-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide;

4-(2-cyclohexen-1-yloxy)-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide;

30 N-(5-isopropyl-1,3-thiazol-2-yl)-4-(trifluoromethoxy)benzamide;

4-(difluoromethoxy)-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide;

N-(5-isopropyl-1,3-thiazol-2-yl)-4-(methylsulfanyl)benzamide;

35 2-[(4-chlorophenyl)sulfinyl]-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide;

N-(5-isopropyl-1,3-thiazol-2-yl)-2-[(4-nitrophenyl)sulfinyl]benzamide;
N-(5-isopropyl-1,3-thiazol-2-yl)-4-[(4-methylphenyl)sulfonyl]-3-nitrobenzamide;
5 N-(5-isopropyl-1,3-thiazol-2-yl)-3-[(trifluoromethyl)sulfanyl]benzamide;
N-(5-isopropyl-1,3-thiazol-2-yl)-2-methoxy-4-(methylsulfanyl)benzamide;
2-[(2-cyanophenyl)sulfanyl]-N-(5-isopropyl-1,3-thiazol-2-
10 yl)benzamide;
N~1~, N~1~-diethyl-3,6-difluoro-N~2~-¹(5-isopropyl-1,3-thiazol-2-yl)phthalamide;
4-formyl-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide;
2-formyl-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide;
15 4-[(2,5-dimethoxyanilino)carbonyl]amino)-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide;
4-(hydroxymethyl)-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide;
4-[(5-isopropyl-1,3-thiazol-2-yl)amino]carbonyl)-2-
20 nitrobenzyl acetate;
4-[(5-isopropyl-1,3-thiazol-2-yl)amino]carbonyl)-2-nitrobenzyl 4-(acetylamino)-3-iodobenzoate;
4-(acetylamino)-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide;
N-(5-isopropyl-1,3-thiazol-2-yl)-4-[(2-
25 phenylacetyl)amino]benzamide;
4-(acetylamino)-3-iodo-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide;
4-amino-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide;
4-(dimethylamino)-N-(5-isopropyl-1,3-thiazol-2-
30 yl)benzamide;
3-(dimethylamino)-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide;
2-(methylamino)-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide;
N-(5-isopropyl-1,3-thiazol-2-yl)-2-[3-
35 (trifluoromethyl)anilino]benzamide;
3-[(5-bromo-1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl)methyl]amino)-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide;

WO 00/26202

-72-

5 N-(5-isopropyl-1,3-thiazol-2-yl)-4-(1H-pyrrol-1-yl)benzamide; 2,6-dichloro-N-(5-isopropyl-1,3-thiazol-2-yl)isonicotinamide; 5 2-(4-bromophenyl)-6-(4-iodophenyl)-N-(5-isopropyl-1,3-thiazol-2-yl)isonicotinamide; N-(5-isopropyl-1,3-thiazol-2-yl)anilino)nicotinamide; 10 5,6-dichloro-N-(5-isopropyl-1,3-thiazol-2-yl)nicotinamide; 2-chloro-N-(5-isopropyl-1,3-thiazol-2-yl)-6-methylnicotinamide; 2,6-dichloro-5-fluoro-N-(5-isopropyl-1,3-thiazol-2-yl)-6-yl)nicotinamide; 15 N-(5-isopropyl-1,3-thiazol-2-yl)-2-phenoxy)nicotinamide; N-(5-isopropyl-1,3-thiazol-2-yl)-6-(2,2,2-trifluoroethoxy)nicotinamide; N-(5-isopropyl-1,3-thiazol-2-yl)-2,6-dimethoxynicotinamide; 20 N-(5-isopropyl-1,3-thiazol-2-yl)-2-quinoxalinecarboxamide; N-(5-isopropyl-1,3-thiazol-2-yl)-5-methyl-2-pyrazinecarboxamide; N-(5-isopropyl-1,3-thiazol-2-yl)-8-quinolinecarboxamide; 25 N-(5-isopropyl-1,3-thiazol-2-yl)-2-phenyl-4-quinolinecarboxamide; N-(5-isopropyl-1,3-thiazol-2-yl)-5-methyl-1-phenyl-1H-pyrazole-3-carboxamide; N-(5-isopropyl-1,3-thiazol-2-yl)-1H-pyrazole-4-carboxamide; 30 1,2,3-triazole-4-carboxamide; 2-[(2,1,3-benzoxadiazol-5-yl)oxy]methyl]-N-(5-isopropyl-1,3-thiazol-2-yl)-5-methyl-2-phenyl-1H-pyrazole-3- N-(5-isopropyl-1,3-thiazol-2-yl)-9H-fluorene-1-carboxamide; 35 N-(5-isopropyl-1,3-thiazol-2-yl)-7-methoxy-1-benzofuran-2-carboxamide; N-(5-isopropyl-1,3-thiazol-2-yl)-1-[4-methylphenyl]sulfonyl]-1H-pyrrole-3-carboxamide; 2-ethoxy-N-(5-isopropyl-1,3-thiazol-2-yl)-1-naphthamide;

4-fluoro-N-(5-isopropyl-1,3-thiazol-2-yl)-1-naphthamide;
N-(5-isopropyl-1,3-thiazol-2-yl)-2-naphthamide;
N-(5-isopropyl-1,3-thiazol-2-yl)-9,10-dioxo-9,10-dihydro-2-anthracenecarboxamide;

5 N-(5-isopropyl-1,3-thiazol-2-yl)-9-oxo-9H-fluorene-4-carboxamide
N-(5-isopropyl-1,3-thiazol-2-yl)-9-oxo-9H-fluorene-1-carboxamide;
N-(5-isopropyl-1,3-thiazol-2-yl)-8-oxo-5,6,7,8-tetrahydro-10-2-naphthalenecarboxamide;

N-(5-isopropyl-1,3-thiazol-2-yl)-1,3-dioxo-1,3-dihydro-2-benzofuran-5-carboxamide;
N-(5-isopropyl-1,3-thiazol-2-yl)-1H-indole-5-carboxamide;
N-(5-isopropyl-1,3-thiazol-2-yl)-1H-indole-4-carboxamide;

15 N-(5-isopropyl-1,3-thiazol-2-yl)-1-methyl-2-phenyl-1H-indole-5-carboxamide;
2-butyl-N-(5-isopropyl-1,3-thiazol-2-yl)-1-methyl-1H-indole-5-carboxamide;
N-(5-isopropyl-1,3-thiazol-2-yl)-1H-indole-6-carboxamide;

20 N-(5-isopropyl-1,3-thiazol-2-yl)-5-methoxy-1H-indole-2-carboxamide;
1-allyl-2-butyl-N-(5-isopropyl-1,3-thiazol-2-yl)-1H-indole-5-carboxamide;
N-(5-isopropyl-1,3-thiazol-2-yl)-1-methyl-1H-indole-2-carboxamide;

25 1-benzyl-N-(5-isopropyl-1,3-thiazol-2-yl)-2-phenyl-1H-indole-5-carboxamide;
N-(5-isopropyl-1,3-thiazol-2-yl)-1H-1,2,3-benzotriazole-5-carboxamide;

30 N-(5-isopropyl-1,3-thiazol-2-yl)-3,5-dimethyl-4-isoxazolecarboxamide;
N-(5-isopropyl-1,3-thiazol-2-yl)-3-thiophenecarboxamide;
N-(5-isopropyl-1,3-thiazol-2-yl)-3-methyl-2-thiophenecarboxamide;

35 N-(5-isopropyl-1,3-thiazol-2-yl)-5-methyl-2-thiophenecarboxamide;
5-bromo-N-(5-isopropyl-1,3-thiazol-2-yl)-2-thiophenecarboxamide;

N-(5-isopropyl-1,3-thiazol-2-yl)-3-[(2,3,3-trichloroacryloyl)amino]-2-thiophenecarboxamide;
N-(5-isopropyl-1,3-thiazol-2-yl)-2-furamide;
N-(5-isopropyl-1,3-thiazol-2-yl)-5-(4-nitrophenyl)-2-furamide;
N-(5-isopropyl-1,3-thiazol-2-yl)-5-(2-nitrophenyl)-2-furamide;
5-(4-chlorophenyl)-N-(5-isopropyl-1,3-thiazol-2-yl)-2-furamide;
10 N-(5-isopropyl-1,3-thiazol-2-yl)-5-[3-(trifluoromethyl)phenyl]-2-furamide;
5-(4-chloro-2-nitrophenyl)-N-(5-isopropyl-1,3-thiazol-2-yl)-2-furamide;
N-(5-isopropyl-1,3-thiazol-2-yl)-5-(4-methyl-2-nitrophenyl)-2-furamide
15 5-[2-chloro-5-(trifluoromethyl)phenyl]-N-(5-isopropyl-1,3-thiazol-2-yl)-2-furamide;
tert-butyl (1S)-2-[(5-isopropyl-1,3-thiazol-2-yl)amino]-1-methyl-2-oxoethylcarbamate
20 tert-butyl (1S,2S)-1-{{(5-isopropyl-1,3-thiazol-2-yl)amino}carbonyl}-2-methylbutylcarbamate
tert-butyl 2-[(5-isopropyl-1,3-thiazol-2-yl)amino]-2-oxoethylcarbamate
tert-butyl (1S)-5-amino-1-{{(5-isopropyl-1,3-thiazol-2-yl)amino}carbonyl}pentylcarbamate
25 tert-butyl 4-[(imino{[(4-methylphenyl)sulfonyl]amino}methyl)amino]-1-{{(5-isopropyl-1,3-thiazol-2-yl)amino}carbonyl}butylcarbamate
tert-butyl 1-{{(5-isopropyl-1,3-thiazol-2-yl)amino}carbonyl}-3-(tritylamino)propylcarbamate
30 tert-butyl (1S)-1-(benzyloxymethyl)-2-[(5-isopropyl-1,3-thiazol-2-yl)amino]-2-oxoethylcarbamate
tert-butyl (1S)-1-benzyl-2-[(5-isopropyl-1,3-thiazol-2-yl)amino]-2-oxoethylcarbamate
35 tert-butyl (1R)-2-[(5-isopropyl-1,3-thiazol-2-yl)amino]-2-oxo-1-(benzylthiomethyl)ethylcarbamate
benzyl (3S)-3-[(tert-butoxycarbonyl)amino]-4-[(5-isopropyl-1,3-thiazol-2-yl)amino]-4-oxobutanoate

tert-butyl (2S)-2-{{(5-isopropyl-1,3-thiazol-2-yl)amino}carbonyl}-1-pyrrolidinecarboxylate

tert-butyl (1S)-1-(1H-indol-3-ylmethyl)-2-[(5-isopropyl-1,3-thiazol-2-yl)amino]-2-oxoethylcarbamate

5 tert-butyl (1S)-1-{{(5-isopropyl-1,3-thiazol-2-yl)amino}carbonyl}-3-(methylsulfanyl)propylcarbamate

tert-butyl (1S)-2-benzyloxy-1-{{(5-isopropyl-1,3-thiazol-2-yl)amino}carbonyl}propylcarbamate

tert-butyl (1S)-1-(4-benzyloxybenzyl)-2-[(5-isopropyl-1,3-thiazol-2-yl)amino]-2-oxoethylcarbamate

10 tert-butyl (1S)-1-{{(5-isopropyl-1,3-thiazol-2-yl)amino}carbonyl}-2-methylpropylcarbamate

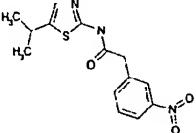
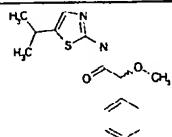
tert-butyl (1S)-1-{{(5-isopropyl-1,3-thiazol-2-yl)amino}carbonyl}-3-methylbutylcarbamate and

15 benzyl (4S)-4-[(tert-butoxycarbonyl)amino]-5-[(5-isopropyl-1,3-thiazol-2-yl)amino]-5-oxopentanoate.

Following the same procedure as reported in Example 3, the compounds described in the table (I) below can be prepared:

20

Table I

MOLSTRUCTURE	m p °C	¹ H-NMR	Sol vent
		12.23 (s broad, 1H, <u>NHCOCH₂</u>), 8.22-7.62 (m, 4H, Ar), 7.15 (s, 1H, H ₄ thiaz), 3.91 (s, 2H, <u>NHCOCH₂</u>), 3.08 (m, 1H, <u>CHMe₂</u>), 1.22 (d, 6H, <u>CHMe₂</u>)	DMSO-d ⁶
		9.81 (s broad, 1H, <u>NHCOCH₂</u>), 7.5- 7.3 (m, 4H, Ar), 7.11 (s, 1H, H ₄ thiaz), 4.83 (s, 1H, <u>NHCOCH</u>), 3.44 (s, 3H, Ome) 3.11 (m, 1H, <u>CHMe₂</u>), 1.3 (d, 6H, <u>CHMe₂</u>)	DMSO-d ⁶

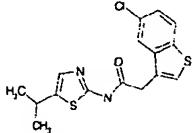
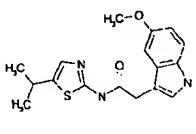
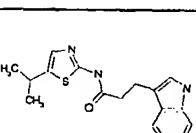
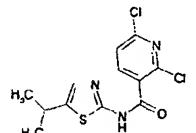
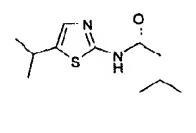
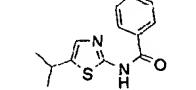
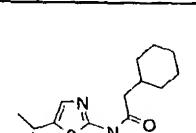
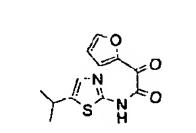
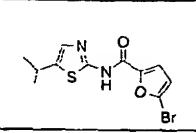
	124 - 125	12.06 (s broad, 1H, NHCO), 7.13 (s, 1H, H4thiaz), 6.92-6.81 (m, 3H, Ar), 3.72 (s, 3H, OMe), 3.70 (s, 3H, OMe), 3.61 (s, 2H, NHCOCH ₂), 3.07 (m, 1H, CHMe ₂), 1.22 (d, 6H, CHMe ₂)	DMSO-d ⁶
	77 - 78	12.05 (s broad, 1H, NHCO), 7.38-7.29 (m, 5H, Ar), 7.12 (s, 1H, H4thiaz), 4.95 (s, 1H, CHOMe), 3.23 (s, 2H, CHOMe), 3.05 (m, 1H, CHMe ₂), 1.20 (d, 6H, CHMe ₂)	DMSO-d ⁵
	136 - 137	12.08 (s broad, 1H, NHCOCH ₂), 7.28 (d, 2H, Ar), 7.13 (s, 1H, H4thiaz), 7.1 (d, 2H, Ar), 3.65 (s, 2H, NHCOCH ₂), 3.06 (m, 1H, CHMe ₂), 2.98 (s, 6H, NMe ₂), 1.22 (d, 6H, CHMe ₂)	DMSO-d ⁶
	130 - 131	12.22 (s, 1H, NHCO), 7.85-7.48 (m, 7H, Ar), 7.14 (s, 1H, H4thiaz), 3.89 (s, 2H, CH ₂ CO), 3.07 (m, 1H, CHMe ₂), 1.22 (d, 6H, CHMe ₂)	DMSO-d ⁶
	130 - 131	12.16 (s, 1H, NHCO), 7.52-7.29 (m, 4H, Ar), 7.14 (s, 1H, H4thiaz), 3.73 (s, 2H, CH ₂ CO), 3.08 (m, 1H, CHMe ₂), 1.22 (d, 6H, CHMe ₂)	DMSO-d ⁶
	177 - 178	8.07-7.48 (m, 7H, Ar), 7.15 (s, 1H, H4thiaz), 4.22 (s, 2H, CH ₂ CO), 3.06 (m, 1H, CHMe ₂), 1.20 (d, 6H, CHMe ₂)	DMSO-d ⁶
	223 - 224	12.61 (s, 1H, NHCO), 7.69-7.51 (m, 4H, Ar), 7.19 (s, 1H, H4thiaz), 4.55 (dd, 1H, CHCO), 3.08 (m, 1H, CHMe ₂), 2.89 (m, 2H, COCH ₂ CH), 1.22 (d, 6H, CHMe ₂)	DMSO-d ⁶
	105 - 106	12.50 (s, 1H, NHCO), 7.53-7.51 (m, 5H, Ar), 7.18 (s, 1H, H4thiaz), 6.12 (d, 1H, J _{H-F} = 46.8, CHF), 3.09 (m, 1H, CHMe ₂), 1.22 (d, 6H, CHMe ₂)	DMSO-d ⁶
	150 - 152	11.20 (s broad, 1H, NHCO), 7.28-7.07 (m, 5H, Ar+H4thiaz), 3.80 (s, 2H, CH ₂ CO), 3.13 (m, 1H, CHMe ₂), 1.32 (d, 6H, CHMe ₂)	DMSO-d ⁶

	164 - 166	11.45 (s broad, 1H, <u>NHCO</u>), 7.37-7.14 (m, 5H, Ar+ H4thiaz), 3.88 (s, 2H, <u>NHCOCH₂</u>), 3.12 (m, 1H, <u>CHMe₂</u>), 1.32 (d, 6H, <u>CHMe₂</u>)	DMSO-d ⁶
	98-100	8.35 (s broad, 1H, <u>NHCO</u>), 7.40 (m, 5H, Ar), 6.99 (s, 1H, H4thiaz), 3.10 (m, 1H, <u>CHMe₂</u>), 1.78 (m, 2H, <u>CH₂</u>), 1.29 (m, 2H, <u>CH₂</u>), 1.25 (d, 6H, <u>CHMe₂</u>)	CDCl ₃
	130 - 132	12.06 (s broad, 1H, <u>NHCOCH₂</u>), 7.13 (s, 1H, H4thiaz), 6.86-6.75 (m, 3H, Ar), 5.96 (s, 2H, <u>OCH₂O</u>), 3.60 (s, 2H, <u>NHCOCH₂</u>), 3.05 (m, 1H, <u>CHMe₂</u>), 1.22 (d, 6H, <u>CHMe₂</u>)	DMSO-d ⁶
	100 - 102	12.1 (s broad, 1H, <u>NHCOCH₂</u>), 7.2-7 (m, 4H, Ar+ H4thiaz), 3.64 (s, 2H, <u>NHCOCH₂</u>), 3.07 (m, 1H, <u>CHMe₂</u>), 2.8-1.97 (m, 6H, -CH ₂ CH ₂ CH ₂ -), 1.22 (d, 6H, <u>CHMe₂</u>)	DMSO-d ⁶
	98-100	12.06 (s broad, 1H, <u>NHCO</u>), 7.3 (m, 5H, Ar), 7.03 (s, 1H, H4thiaz), 3.79 (q, 1H, <u>CHMe</u>), 3.10 (m, 1H, <u>CHMe₂</u>), 1.59 (d, 3H, <u>CHMe</u>), 1.30 (d, 6H, <u>CHMe₂</u>)	DMSO-d ⁶
	167 - 169	10 (s broad, 1H, <u>NHCOCH₂</u>), 7.6-7.4 (m, 9H, Ar), 7.04 (s, 1H, H4thiaz), 3.84 (s, 2H, <u>NHCOCH₂</u>), 3.11 (m, 1H, <u>CHMe₂</u>), 1.31 (d, 6H, <u>CHMe₂</u>)	DMSO-d ⁶
	115 - 116	12.06 (s broad, 1H, <u>NHCO</u>), 7.26 (m, 5H, Ar), 6.99 (s, 1H, H4thiaz), 3.79 (q, 1H, <u>CHMe</u>), 3.10 (m, 1H, <u>CHMe₂</u>), 1.59 (d, 3H, <u>CHMe</u>), 1.30 (d, 6H, <u>CHMe₂</u>)	DMSO-d ⁶
	112 - 114	12.06 (s broad, 1H, <u>NHCO</u>), 7.33 (m, 5H, Ar), 7.11 (s, 1H, H4thiaz), 3.93 (q, 1H, <u>CHMe</u>), 3.07 (m, 1H, <u>CHMe₂</u>), 1.40 (d, 3H, <u>CHMe</u>), 1.22 (d, 6H, <u>CHMe₂</u>)	DMSO-d ⁶
	124 - 126	12.01 (s broad, 1H, <u>NHCO</u>), 7.11-6-65 (m, 5H, Ar+H4thiaz), 3.55 (s, 2H, <u>NHCOCH₂</u>), 2.83 (s, 6H, <u>NMe₂</u>), 2.56 (d, 2H, <u>CH₂iPr</u>), 1.74 (m, 1H, <u>CHMe₂</u>), 0.87 (d, 6H, <u>CHMe₂</u>)	DMSO-d ⁶

	139 - 141	9.90 (s broad, 1H, <u>NHCO</u>), 7.04 (s, 1H, H4thiaz), 6.78 (m, 3H, Ar), 5.96 (s, 2H, <u>OCH₂O</u>), 3.72 (s, 2H, <u>NHCOCH₂</u>), 2.60 (d, 2H, CH ₂ iPr), 1.85 (m, 1H, <u>CHMe₂</u>), 0.93 (d, 6H, <u>CHMe₂</u>)	CDCl ₃
	175 - 177	12.0 (s broad, 1H, <u>NHCO</u>), 7.28 (m, 6H, <u>CH₂Ph+H4thiaz</u>), 7.08-6.64 (m, 4H, Ar), 4.04 (s, 2H, <u>CH₂Ph</u>), 3.53 (s, 2H, <u>NHCOCH₂</u>), 2.82 (s, 6H, <u>NMe₂</u>)	DMSO-d ^b
	88- 90	12.08 (s broad, 1H, <u>NHCO</u>), 7.20-6.81 (m, 5H, Ar+H4thiaz), 4.01 (dd, 2H, <u>OCH₂CH₂OMe</u>), 3.68 (s, 2H, <u>NHCOCH₂</u>), 3.61 (dd, 2H, <u>OCH₂CH₂OMe</u>), 3.3 (s, 3H, <u>OCH₂CH₂OMe</u>), 3.05 (m, 1H, <u>CHMe₂</u>), 1.22 (s, 6H, <u>CHMe₂</u>)	DMSO-d ^b
	230 - 231	12.81 (s broad, 1H, <u>NHCO</u>), 8.63-7.79 (m, 3H, Ar), 7.71 (s, 2H, NH ₂), 7.24 (s, 1H, H4thiaz), 3.12 (m, 1H, <u>CHMe₂</u>), 1.27 (d, 6H, <u>CHMe₂</u>)	DMSO-d ^b
	181 - 182	12.47 (s broad, 1H, <u>NHCO</u>), 8.13-7.37 (m, 4H, Ar), 7.23 (s, 1H, H4thiaz), 3.13 (m, 1H, <u>CHMe₂</u>), 1.27 (d, 6H, <u>CHMe₂</u>)	DMSO-d ^b
	263 - 264	12.0 (s broad, 1H, <u>NHCO</u>), 8.89-7.82 (m, 4H, Ar), 7.27 (s, 1H, H4thiaz), 3.13 (m, 1H, <u>CHMe₂</u>), 1.28 (d, 6H, <u>CHMe₂</u>)	DMSO-d ^b
	204 - 206	12.6 (s broad, 1H, <u>NHCO</u>), 8.06-7.60 (m, 3H, Ar), 7.23 (s, 1H, H4thiaz), 3.12 (m, 1H, <u>CHMe₂</u>), 1.27 (d, 6H, <u>CHMe₂</u>)	DMSO-d ^b
	148 - 150	8.54-8.31 (m, 3H, Ar), 6.98 (s, 1H, H4thiaz), 3.43 (s, 3H, SO ₂ Me), 3.14 (m, 1H, <u>CHMe₂</u>), 1.35 (d, 6H, <u>CHMe₂</u>)	CDCl ₃

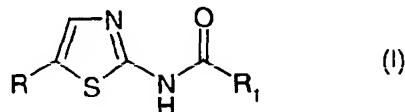
	173 - 175	8.16-8.06 (2d, 4H, Ar), 7.25 (s, 1H, H4thiaz), 3.88 (s, 3H, COOMe), 3.14 (m, 1H, CHMe ₂), 1.28 (d, 6H, CHMe ₂)	DMSO-d ⁶
	164 - 166	8.50-7.86 (m, 3H, Ar), 7.24 (s, 1H, H4thiaz), 3.15 (m, 1H, CHMe ₂), 1.28 (d, 6H, CHMe ₂)	DMSO-d ⁶
	178 - 179	12.4 (s broad, 1H, NHCO), 8.12-7.21 (m, 3H, Ar), 7.22 (s, 1H, H4thiaz), 3.2-2.48 (m, 5H, CHMe ₂ , + piperazine), 2.22 (s, 3H, NMe), 1.27 (d, 6H, CHMe ₂)	DMSO-d ⁶
		12.6 (s broad, 1H, NHCO), 7.73-7.57 (m, 3H, Ar), 7.22 (s, 1H, H4thiaz), 3.15 (m, 1H, CHMe ₂), 1.27 (d, 6H, CHMe ₂)	DMSO-d ⁶
	207 - 209	12.6 (s broad, 1H, NHCO), 8.16-8.05 (m, 4H, Ar), 7.24 (s, 1H, H4thiaz), 3.13 (m, 1H, CHMe ₂), 2.62 (s, 3H, COMe), 1.28 (d, 6H, CHMe ₂)	DMSO-d ⁶
		9.4 (s broad, 1H, NHCO), 8.3 (s, 1H, NH), 7.55-6.98 (m, 6H, indole+H4thiaz), 3.96 (s, 2H, COCH ₂), 3.10 (m, 1H, CHMe ₂), 1.30 (d, 6H, CHMe ₂)	CDCl ₃
	116 - 118	9.80 (s broad, 1H, NHCO), 7.37-7.05 (m, 3H, Ar), 7.04 (d, 1H, H4thiaz), 3.84 (s, 2H, COCH ₂), 3.11 (m, 1H, CHMe ₂), 1.32 (d, 6H, CHMe ₂)	CDCl ₃
	148 - 150	10.20 (s broad, 1H, NHCO), 7.28-7.01 (m, 4H, Ar+H4thiaz), 4.02 (s, 2H, COCH ₂), 3.13 (m, 1H, CHMe ₂), 1.32 (d, 6H, CHMe ₂)	CDCl ₃
	170 - 172	12.05 (s broad, 1H, NHCO), 10.82 (s, 1H, NH), 7.48-6.90 (m, 5H, indole+H4thiaz), 3.74 (s, 2H, COCH ₂), 3.06 (m, 1H, CHMe ₂), 2.36 (s, 3H, Me), 1.21 (d, 6H, CHMe ₂)	DMSO-d ⁶
	163 - 165	12.07 (s broad, 1H, NHCO), 7.57-7.01 (m, 6H, indole+H4thiaz), 3.79 (s, 2H, COCH ₂), 3.74 (s, 3H, NMe), 3.05 (m, 1H, CHMe ₂), 1.21 (d, 6H, CHMe ₂)	DMSO-d ⁶

	155 - 157	10.20 (s broad, 1H, NHCO), 7.88-7.40 (m, 5H, Ar), 6.95 (s, 1H, H4thiaz), 4.04 (s, 2H, COCH ₂), 3.07 (m, 1H, CHMe ₂), 1.27 (d, 6H, CHMe ₂)	DMSO-d ⁶
	234 - 236	11.3 (s broad, 1H, NHCO), 7.52-6.28 (m, 5H, Ar+H4thiaz), 3.93 (s, 2H, COCH ₂), 3.87 (s, 3H, OMe), 3.10 (m, 1H, CHMe ₂), 1.27 (d, 6H, CHMe ₂)	DMSO-d ⁶
	161 - 163	12.19 (s, 1H, NHCO), 8.49-7.34 (m, 4H, Ar), 7.12 (s, 1H, H4thiaz), 2.56 (d, 2H, CH ₂ iPr), 1.75 (m, 1H, CHMe ₂), 0.86 (d, 6H, CHMe ₂)	DMSO-d ⁶
	166 - 168	12.20 (s, 1H, NHCO), 8.48-7.24 (m, 10H, 2Xar+H4thiaz), 4.06 (s, 2H, CH ₂ Ph), 3.77 (s, 2H, CH ₂ CO)	DMSO-d ⁶
	164 - 167	8.63-7.9 (m, 5H, Ar), 7.11 (s, 1H, H4thiaz), 3.85 (s, 2H, COCH ₂), 3.15 (m, 1H, CHMe ₂), 1.29 (d, 6H, CHMe ₂)	CDCl ₃
	114 - 117	11.6 (s broad, 1H, NHCO), 7.10 (s, 1H, H4thiaz), 3.67 (s, 3H, CH ₃ OCO), 3.15 (m, 1H, CHMe ₂), 2.60 (m, 2H, CH ₂ CH ₂ CH ₂), 2.46 (m, 2H, CH ₂ CH ₂ CH ₂), 2.09 (m, 2H, CH ₂ CH ₂ CH ₂), 1.34 (d, 6H, CHMe ₂)	CDCl ₃
	217 - 220	10.6 (s broad, 1H, NHCO), 7.36 (m, 5H, Ar), 7.10 (s, 1H, H4thiaz), 6.61 (d, 1H, J=15.8, CH=CHPh), 6.36 (dt, 1H, J=15.8, 7.3, CH=CHPh), 3.43 (dd, 2H, J=7.3, 1.3, COCH ₂), 3.14 (m, 1H, CHMe ₂), 1.33 (d, 6H, CHMe ₂)	CDCl ₃
	222 - 225 dec .	12.09 (s broad, 1H, NHCO), 11.5 (s, 1H, NH), 7.78-7.16 (m, 4H, indole), 7.13 (s, 1H, H4thiaz), 3.78 (s, 2H, COCH ₂), 3.07 (m, 1H, CHMe ₂), 1.21 (d, 6H, CHMe ₂)	DMSO-d ⁶
	222 - 225 dec .	12.07 (s, 1H, NHCO), 11.03 (s, 1H, NH), 7.3-6.80 (m, 5H, indole+H4thiaz), 3.77 (s, 2H, COCH ₂), 3.06 (m, 1H, CHMe ₂), 1.22 (d, 6H, CHMe ₂)	DMSO-d ⁶

	172 - 173	12.25 (s, 1H, <u>NHCO</u>), 8.02-7.4 (m, 4H, Ar), 7.15 (s, 1H, H4thiaz), 4.0 (s, 2H, COCH ₂), 3.07 (m, 1H, CHMe ₂), 1.22 (d, 6H, CHMe ₂)	DMSO-d ⁶
	203 - 204	12.05 (s, 1H, <u>NHCO</u>), 10.77 (s, 1H, NH), 7.22-6.70 (m, 5H, indole+ H4thiaz), 3.75 (s, 2H, COCH ₂), 3.72 (s, 3H, OMe), 3.07 (m, 1H, CHMe ₂), 1.22 (d, 6H, CHMe ₂)	DMSO-d ⁶
	163 - 164	12.89 (s, 1H, <u>NHCO</u>), 10.75 (s, 1H, NH), 7.12-6.97 (m, 5H, indole+ H4thiaz), 3.10 (m, 1H, CHMe ₂), 3.01 (t, 2H, CH ₂ CH ₂ CO), 2.78 (t, 2H, CH ₂ CH ₂ CO), 1.25 (d, 6H, CHMe ₂)	DMSO-d ⁶
	186 - 187	12.7 (s broad, 1H, <u>NHCO</u>), 8.18 (d, 1H, J=7.8, Ar), 7.71 (d, 1H, J=7.8, Ar), 7.24 (s, 1H, H4thiaz), 3.15 (m, 1H, CHMe ₂), 1.27 (d, 6H, CHMe ₂)	DMSO-d ⁶
		10.8 (s broad, 1H, <u>NHCO</u>), 7.45 (s, 1H, H4thiaz), 3.33 (m, 1H, CHMe ₂), 2.54 (m, 2H, CH ₂ CHMe ₂), 2.42 (m, 1H, CH ₂ CHMe ₂), 1.53 (d, 6H, CH ₂ CHMe ₂), 1.21 (d, 6H, CHMe ₂)	CDCl ₃
		12.4 (s broad, 1H, <u>NHCO</u>), 8.05-7.51 (m, 5H, Ph), 7.23 (s, 1H, H4thiaz), 3.13 (m, 1H, CHMe ₂), 1.28 (d, 6H, CHMe ₂)	DMSO-d ⁶
		11.8 (s broad, 1H, <u>NHCO</u>), 7.11 (s, 1H, H4thiaz), 3.08 (m, 1H, CHMe ₂), 2.25 (d, 2H, CH ₂ CO), 2.42 (m, 1H, CH ₂ CHMe ₂), 1.23 (d, 6H, CHMe ₂), 1.8-0.8 (m, 11H, cyclohexyl)	DMSO-d ⁶
		8.13 (d, 1H, H3fur), 7.84 (d, 1H, H5fur), 7.25 (d, 1H, H4thiaz), 6.69 (dd, 1H, H4fur), 7.45 (s, 1H, H4thiaz), 3.20 (m, 1H, CHMe ₂), 1.39 (d, 6H, CHMe ₂)	CDCl ₃
		12.7 (s broad, 1H, <u>NHCO</u>), 7.54-6.82 (m, 3H, H4thiaz+furane), 3.10 (m, 1H, CHMe ₂), 1.26 (d, 6H, CHMe ₂)	DMSO-d ⁶

CLAIMS

1. The use of a compound which is a 2-amino-1,3-thiazole derivative of formula (I)



5 wherein

R is a halogen atom, a nitro group, an optionally substituted amino group or it is a group, optionally further substituted, selected from:

10 i) straight or branched C₁-C₈ alkyl, C₂-C₆ alkenyl or C₂-C₆ alkynyl;

ii) C₃-C₆ cycloalkyl;

iii) aryl or arylalkyl with from 1 to 8 carbon atoms within the straight or branched alkyl chain;

15 R₁ is an optionally further substituted group selected from:

i) straight or branched C₁-C₈ alkyl or C₂-C₆ alkenyl;

ii) 3 to 6 membered carbocycle or 5 to 7 membered heterocycle ring;

iii) aryl or arylcarbonyl;

20 iv) arylalkyl with from 1 to 8 carbon atoms within the straight or branched alkyl chain;

v) arylalkenyl with from 2 to 6 carbon atoms within the straight or branched alkenyl chain;

vi) an optionally protected amino acid residue;

25 or a pharmaceutically acceptable salt thereof; in the manufacture of a medicament for treating cell proliferative disorders associated with an altered cell dependent kinase activity.

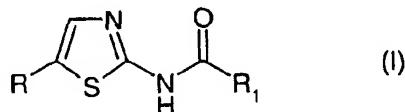
30 2. Use according to claim 1 wherein the said cell proliferative disorder is selected from the group consisting of cancer, Alzheimer's disease, viral infections, auto-immune diseases or neurodegenerative disorders.

3. Use according to claim 2 wherein the cancer is selected from the group consisting of carcinoma, squamous cell carcinoma, hematopoietic tumors of myeloid or lymphoid lineage, tumors of mesenchymal origin, tumors of the 5 central and peripheral nervous system, melanoma, seminoma, teratocarcinoma, osteosarcoma, xenoderoma pigmentosum, keratoctanthoma, thyroid follicular cancer and Kaposi's sarcoma.

10 4. Use according to claim 1 wherein the cell proliferative disorder is selected from the group consisting of benign prostate hyperplasia, familial adenomatosis polyposis, neuro-fibromatosis, psoriasis, vascular smooth cell proliferation associated with 15 atherosclerosis, pulmonary fibrosis, arthritis glomerulonephritis and post-surgical stenosis and restenosis.

5. Use according to any one of the preceding claims 20 wherein the medicament enables tumor angiogenesis and metastasis inhibition.

6. A compound which is a 2-amino-1,3-thiazole derivative of formula (I)



25

wherein

R is a halogen atom, a nitro group, an optionally substituted amino group or it is a group, optionally further substituted, selected from:

30 i) straight or branched C₁-C₈ alkyl, C₂-C₆ alkenyl or C₂-C₆ alkynyl;

ii) C₃-C₆ cycloalkyl;

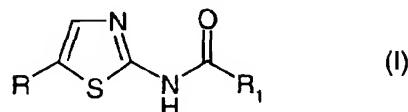
iii) aryl or arylalkyl with from 1 to 8 carbon atoms within the straight or branched alkyl chain;

R_1 is an optionally further substituted group selected from:

- i) straight or branched C_1 - C_8 alkyl or C_2 - C_6 alkenyl;
- ii) 3 to 6 membered carbocycle or 5 to 7 membered 5 heterocycle ring;
- iii) aryl or arylcarbonyl;
- iv) arylalkyl with from 1 to 8 carbon atoms within the straight or branched alkyl chain;
- v) arylalkenyl with from 2 to 6 carbon atoms within the straight or branched alkenyl chain;
- vi) an optionally protected amino acid residue;

or a pharmaceutically acceptable salt thereof; for use as a medicament; provided that each of R and R_1 , independently, is not a methyl group and that the compound is not 2-diethylaminomethyl-carbonylamino-5-chloro-1,3-thiazole.

7. A compound which is a 2-amino-1,3-thiazole derivative of formula (I)



20 wherein

R is a halogen atom, a nitro group, an optionally substituted amino group or it is a group, optionally further substituted, selected from:

- i) straight or branched C_1 - C_8 alkyl, C_2 - C_6 alkenyl or C_2 - C_6 alkynyl;

- ii) C_1 - C_6 cycloalkyl;
- iii) aryl or arylalkyl with from 1 to 8 carbon atoms within the straight or branched alkyl chain;

R_1 is an optionally further substituted group selected 30 from:

- i) straight or branched C_1 - C_8 alkyl or C_2 - C_6 alkenyl;
- ii) 3 to 6 membered carbocycle or 5 to 7 membered heterocycle ring;

- iii) aryl or arylcarbonyl;

- iv) arylalkyl with from 1 to 8 carbon atoms within the straight or branched alkyl chain;

- v) arylalkenyl with from 2 to 6 carbon atoms within the straight or branched alkenyl chain;
- vi) an optionally protected amino acid residue; or a pharmaceutically acceptable salt thereof;

5 provided that:

- a) R and R₁, each independently, are not methyl;
- b) when R is bromine or chlorine then, R₁ is not unsubstituted C₂-C₄ alkyl or an optionally substituted aminomethyl;

10 c) when R is nitro or phenyl, then R₁ is not unsubstituted phenyl.

8. A compound of formula (I), according to claim 7, wherein R is a halogen atom or an optionally substituted group selected from a straight or branched C₁-C₄ alkyl, C₃-C₆ cycloalkyl, aryl or an arylalkyl with from 1 to 4 carbon atoms within the alkyl chain; R₁ is an optionally substituted group selected from straight or branched C₁-C₄ alkyl or alkenyl, aryl or arylalkyl with from 1 to 4 carbon atoms within the alkyl chain or it is an optionally protected amino acid residue.

9. A compound of formula (I), according to claim 8, wherein R is a bromine or chlorine atom or is an optionally substituted group selected from straight or branched C₁-C₄ alkyl, cyclopropyl, aryl or arylalkyl with from 1 to 2 carbon atoms within the alkyl chain; R₁ is an optionally substituted group selected from straight or branched C₁-C₄ alkyl or alkenyl, aryl or arylalkyl with from 1 to 4 carbon atoms within the alkyl chain or it is an optionally protected amino acid residue.

10. A compound of formula (I) according to claim 7 wherein R is a halogen atom or is selected from nitro, amino, 35 alkylamino, hydroxyalkylamino, arylamino, C₃-C₆ cycloalkyl and straight or branched C₁-C₆ alkyl which is unsubstituted or substituted by hydroxy, alkylthio,

alkoxy, amino, alkylamino, alkoxy carbonylamino, alkoxy carbonyl alkylamino, alkyl carbonyl, alkylsulfonyl, alkoxy carbonyl, carboxy or aryl which is unsubstituted or substituted by one or more hydroxy, halogen, nitro, 5 alkoxy, aryloxy, alkylthio, arylthio, amino, alkylamino, dialkylamino, N-alkyl-piperazinyl, 4-morpholinyl, arylamino, cyano, alkyl, phenyl, aminosulfonyl, aminocarbonyl, alkyl carbonyl, aryl carbonyl, alkoxy carbonyl or carboxy groups, or R is 10 an aryl group which is unsubstituted or substituted by one or more hydroxy, halogen, nitro, alkoxy, aryloxy, alkylthio, arylthio, amino, alkylamino, dialkylamino, N-alkyl-piperazinyl, 4-morpholinyl, arylamino, cyano, alkyl, phenyl, aminosulphonyl, aminocarbonyl, 15 alkyl carbonyl, aryl carbonyl, alkoxy carbonyl or carboxy groups;

R₁ is a straight or branched C₁-C₆ alkyl group or an aryl group, each being unsubstituted or substituted as defined above for R;
20 or a pharmaceutically acceptable salt thereof;
provided that:
a) R and R₁, each independently, are not methyl;
b) when R is bromine or chlorine then, R₁ is not unsubstituted C₂-C₄ alkyl or an optionally substituted 25 aminomethyl;
c) when R is nitro or phenyl, then R₁ is not unsubstituted phenyl.

11. A compound of formula (I) according to any one of the 30 preceding claims, whenever appropriate in the form of a pharmaceutically acceptable salt, selected from the group consisting of:

1. ethyl 3-[(5-bromo-1,3-thiazol-2-yl)amino]-3-oxopropanoate;
- 35 2. N-(5-bromo-1,3-thiazol-2-yl)-2-phenyl-acetamide;
3. N-(5-bromo-1,3-thiazol-2-yl)-benzamide;

4. Ethyl 4-[(5-bromo-1,3-thiazol-2-yl)amino]-4-oxobutanoate;
5. N-(5-Bromo-thiazol-2-yl)-3-hydroxy-propionamide;
6. N-(5-Bromo-1,3-thiazol-2-yl)-4-hydroxybutanamide;
7. N-(5-Bromo-thiazol-2-yl)-2-ethoxy-acetamide;
8. 2-N-[2-(3-pyridyl)-acetyl-amino]-5-bromo-thiazole;
9. 2-N-[2-(3-pyridyl)-acetyl-amino]-5-isopropyl-thiazole;
10. N-(5-bromo-1,3-thiazol-2-yl)-2-(3-hydroxyphenyl)acetamide;
11. N-(5-isopropyl-1,3-thiazol-2-yl)-2-(3-hydroxyphenyl)acetamide;
12. N-(5-bromo-1,3-thiazol-2-yl)-2-(3-methoxyphenyl)acetamide;
13. N-(5-isopropyl-1,3-thiazol-2-yl)-2-(3-methoxyphenyl)acetamide;
14. N-(5-bromo-1,3-thiazol-2-yl)-2-(3-chorophenyl)acetamide;
15. N-(5-isopropyl-1,3-thiazol-2-yl)-2-(3-chorophenyl)acetamide;
16. N-(5-bromo-1,3-thiazol-2-yl)-2-(4-hydroxyphenyl)acetamide;
17. N-(5-isopropyl-1,3-thiazol-2-yl)-2-(4-hydroxyphenyl)acetamide;
18. N-(5-bromo-1,3-thiazol-2-yl)-2-(3,4-dihydroxyphenyl)acetamide;
19. N-(5-isopropyl-1,3-thiazol-2-yl)-2-(3,4-dihydroxyphenyl)acetamide;
20. N-(5-bromo-1,3-thiazol-2-yl)-2-(4-hydroxy-3-methoxyphenyl)acetamide;
21. N-(5-isopropyl-1,3-thiazol-2-yl)-2-(4-hydroxy-3-methoxyphenyl)acetamide;
22. N-(5-bromo-1,3-thiazol-2-yl)-2-(4-methoxyphenyl)acetamide;
23. N-(5-isopropyl-1,3-thiazol-2-yl)-2-(4-methoxyphenyl)acetamide;
24. N-(5-isopropyl-1,3-thiazol-2-yl)-2-(4-chlorophenyl)acetamide;
25. N-(5-isopropyl-1,3-thiazol-2-yl)-2-phenyl-acetamide;
26. N-(5-bromo-thiazol-2-yl)-4-sulfamoyl-benzamide;

27.N-(5-isopropyl-thiazol-2-yl)-4-sulfamoyl-benzamide;
28.4-amino-N-(5-bromo-1,3-thiazol-2-yl)butanamide;
29.3-amino-N-(5-bromo-1,3-thiazol-2-yl)propionamide;
30.N-(5-isopropyl-1,3-thiazol-2-yl)-butanamide;
5 31.N-(5-bromo-1,3-thiazol-2-yl)-butanamide;
32.N-(5-chloro-1,3-thiazol-2-yl)-butanamide;
33.N-(5-phenyl-1,3-thiazol-2-yl)-butanamide;
34.N-(5-nitro-1,3-thiazol-2-yl)-butanamide;
35.N-(5-methyl-1,3-thiazol-2-yl)-butanamide;
10 36.N-(5-benzyl-1,3-thiazol-2-yl)-butanamide;
37.N-(5-isobutyl-1,3-thiazol-2-yl)-butanamide;
38.N-(5-cyclopropyl-1,3-thiazol-2-yl)-butanamide;
39.N-{5-[2-(methylsulfonyl)ethyl]-1,3-thiazol-2-yl}-
butanamide;
15 40.N-[5-(2-methylthioethyl)-1,3-thiazol-2-yl]-butanamide;
41.N-{5-[2-(methoxycarbonyl)ethyl]-1,3-thiazol-2-yl}-
butanamide;
42.N-[5-(3-methoxy-propyl)-1,3-thiazol-2-yl]-butanamide;
43.N-[5-(2-ethoxy-ethyl)-1,3-thiazol-2-yl]-butanamide;
20 44.N-[5-(indol-3-yl-methyl)-1,3-thiazol-2-yl]-butanamide;
45.N-[5-(3-oxo-buty1)-1,3-thiazol-2 yl]-butanamide;
46.2-[3-(3-chloropropoxy)phenyl]-N-(5-isopropyl-1,3-
thiazol-2-yl)acetamide;
47.2-[3-(2-chloroethoxy)phenyl]-N-(5-isopropyl-1,3-thiazol-
25 2-yl)acetamide;
48.2-(4-aminophenyl)-N-(5-isopropyl-1,3-thiazol-2-
yl)acetamide;
49.4-amino-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide;
50.2-(2-amino-1,3-thiazol-4-yl)-N-(5-isopropyl-1,3-thiazol-
30 2-yl)acetamide;
51.N-(5-isopropyl-1,3-thiazol-2-yl)-2-{3-[3-(4-
morpholinyl)propoxy]phenyl}acetamide;
52.N-(5-isopropyl-1,3-thiazol-2-yl)-2-{3-[2-(4-
morpholinyl)ethoxy]phenyl}acetamide;
35 53.N-(5-isopropyl-1,3-thiazol-2-yl)-2-{3-[3-(1-
pirrolidinyl)propoxy]phenyl}acetamide;

54. N-(5-isopropyl-1,3-thiazol-2-yl)-2-{3-[3-(4-methyl-1-piperazinyl)propoxy]phenyl}acetamide;

55. 2-{3-[2-(dimethylamino)ethoxy]phenyl}-N-(5-isopropyl-1,3-thiazol-2-yl)acetamide;

5 56. 2-{3-[3-(dimethylamino)propoxy]phenyl}-N-(5-isopropyl-1,3-thiazol-2-yl)acetamide

57. 2-[4-(dimethylamino)phenyl]-N-(5-isobutyl-1,3-thiazol-2-yl)acetamide

58. 2-(1,3-benzodioxol-5-yl)-N-(5-isobutyl-1,3-thiazol-2-yl)acetamide

10 59. N-(5-benzyl-1,3-thiazol-2-yl)-2-[4-(dimethylamino)phenyl]acetamide

60. N-(5-isopropyl-1,3-thiazol-2-yl)-2-[3-(2-methoxyethoxy)-phenyl]acetamide

15 61. 3-chloro-N-(5-isopropyl-1,3-thiazol-2-yl)-4-(4-methyl-1-piperazinyl)benzamide

62. N-(5-isobutyl-1,3-thiazol-2-yl)-2-(3-pyridinyl)acetamide

63. N-(5-benzyl-1,3-thiazol-2-yl)-2-(3-pyridinyl)acetamide

64. 2-[N-[2'-N'-(ethoxycarbonyl-methyl)-amino]-acetyl]-

20 amino-5-bromo-thiazole

65. 2-anilino-N-(5-isopropyl-1,3-thiazol-2-yl)acetamide

66. (R)-N-(5-isopropyl-1,3-thiazol-2-yl)-2-phenylpropanamide

67. (S)-N-(5-isopropyl-1,3-thiazol-2-yl)-2-phenylpropanamide

68. N-(5-isopropyl-1,3-thiazol-2-yl)benzamide

25 69. 2,5-dichloro-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide

70. 3,5-dichloro-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide

71. 3,4-dichloro-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide

72. 2,4-dichloro-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide

73. 2,3-dichloro-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide

30 74. 3-iodio-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide

75. 2-iodio-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide

76. 4-iodio-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide

77. 3-bromo-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide

78. 4-chloro-2-fluoro-N-(5-isopropyl-1,3-thiazol-2-

35 yl)benzamide

79. 5-bromo-2-chloro-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide

80. 3-chloro-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide

WO 00/26202

81. 2-chloro-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide
82. 4-chloro-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide
83. 3-fluoro-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide
84. 2-fluoro-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide
85. 4-fluoro-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide
5 86. 2,4-difluoro-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide
87. 3,4,5,6-pentafluoro-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide
88. 2,3,4,5,6-pentafluoro-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide
- 90 -
10 89. N-(5-isopropyl-1,3-thiazol-2-yl)-4-methyl-3-
nitrobenzamide
90. N-(5-isopropyl-1,3-thiazol-2-yl)-5-methyl-2-
nitrobenzamide
15 91. N-(5-isopropyl-1,3-thiazol-2-yl)-3-methyl-2-
nitrobenzamide
92. N-(5-isopropyl-1,3-thiazol-2-yl)-3,5-dimethyl-4-
nitrobenzamide
93. N-(5-isopropyl-1,3-thiazol-2-yl)-4-methoxy-2-
nitrobenzamide
20 94. N-(5-isopropyl-1,3-thiazol-2-yl)-3-methoxy-2-
nitrobenzamide
95. N-(5-isopropyl-1,3-thiazol-2-yl)-4-methoxy-3-
nitrobenzamide
96. N-(5-isopropyl-1,3-thiazol-2-yl)-3-methoxy-4-
nitrobenzamide
25 97. N-(5-isopropyl-1,3-thiazol-2-yl)-3,5-dinitrobenzamide
98. 5-[(5-isopropyl-1,3-thiazol-2-yl)-3,5-dinitrobenzamide
nitrophenyl octanoate
99. N-(5-isopropyl-1,3-thiazol-2-yl)-2-nitrobenzamide
30 100. N-(5-isopropyl-1,3-thiazol-2-yl)-4-nitrobenzamide
101. N-(5-isopropyl-1,3-thiazol-2-yl)-4-(methylsulfonyl)-3-
nitrobenzamide
102. N-(5-isopropyl-1,3-thiazol-2-yl)-4-(methylsulfonyl)-3-
35 103. 4-chloro-N-(5-isopropyl-1,3-thiazol-2-yl)-3-
nitrobenzamide
104. 6-chloro-N-(5-isopropyl-1,3-thiazol-2-yl)-3-
nitrobenzamide

105. 4-chloro-N-(5-isopropyl-1,3-thiazol-2-yl)-2-nitrobenzamide
106. 2-chloro-N-(5-isopropyl-1,3-thiazol-2-yl)-4-nitrobenzamide
- 5 107. 5-chloro-N-(5-isopropyl-1,3-thiazol-2-yl)-2-nitrobenzamide
108. 2-bromo-N-(5-isopropyl-1,3-thiazol-2-yl)-5-nitrobenzamide
109. 4-fluoro-N-(5-isopropyl-1,3-thiazol-2-yl)-3-nitrobenzamide
- 10 110. 4-fluoro-N-(5-isopropyl-1,3-thiazol-2-yl)-2-nitrobenzamide
111. N-(5-isopropyl-1,3-thiazol-2-yl)-2-nitro-4-(trifluoromethyl)benzamide
- 15 112. N-(5-isopropyl-1,3-thiazol-2-yl)-3,5-bis(trifluoromethyl)benzamide
113. N-(5-isopropyl-1,3-thiazol-2-yl)-2,6-bis(trifluoromethyl)benzamide
114. N-(5-isopropyl-1,3-thiazol-2-yl)-2-(trifluoromethyl)benzamide
- 20 115. N-(5-isopropyl-1,3-thiazol-2-yl)-3-(trifluoromethyl)benzamide
116. 3-fluoro-N-(5-isopropyl-1,3-thiazol-2-yl)-4-(trifluoromethyl)benzamide
- 25 117. 2-fluoro-N-(5-isopropyl-1,3-thiazol-2-yl)-3-(trifluoromethyl)benzamide
118. 5-fluoro-N-(5-isopropyl-1,3-thiazol-2-yl)-3-(trifluoromethyl)benzamide
119. 2-fluoro-N-(5-isopropyl-1,3-thiazol-2-yl)-4-(trifluoromethyl)benzamide
- 30 120. 4-fluoro-N-(5-isopropyl-1,3-thiazol-2-yl)-3-(trifluoromethyl)benzamide
121. methyl 4-{{(5-isopropyl-1,3-thiazol-2-yl)amino}carbonyl}benzoate
- 35 122. methyl 2-{{(5-isopropyl-1,3-thiazol-2-yl)amino}carbonyl}benzoate
123. 4-cyano-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide
124. 3-cyano-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide

125. N-(5-isopropyl-1,3-thiazol-2-yl)-3-methylbenzamide
126. N-(5-isopropyl-1,3-thiazol-2-yl)-2-methylbenzamide
127. N-(5-isopropyl-1,3-thiazol-2-yl)-4-methylbenzamide
128. N-(5-isopropyl-1,3-thiazol-2-yl)-4-vinylbenzamide
- 5 129. N-(5-isopropyl-1,3-thiazol-2-yl)-4-(2-phenylethynyl)benzamide
130. N-(5-isopropyl-1,3-thiazol-2-yl)-3-methoxy-4-methylbenzamide
131. 2-benzyl-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide
- 10 132. N-(5-isopropyl-1,3-thiazol-2-yl)-2-phenethylbenzamide
133. N-(5-isopropyl-1,3-thiazol-2-yl)-2-phenylbenzamide
134. N-(5-isopropyl-1,3-thiazol-2-yl)-4-phenylbenzamide
135. 4-(tert-butyl)-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide
- 15 136. N-(5-isopropyl-1,3-thiazol-2-yl)-4-isopropylbenzamide
137. N-(5-isopropyl-1,3-thiazol-2-yl)-4-pentylbenzamide
138. 3-fluoro-N-(5-isopropyl-1,3-thiazol-2-yl)-4-methylbenzamide
139. N-(5-isopropyl-1,3-thiazol-2-yl)-3,4-dimethylbenzamide
- 20 140. N-(5-isopropyl-1,3-thiazol-2-yl)-3,5-dimethylbenzamide
141. 4-acetyl-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide
142. N-(5-isopropyl-1,3-thiazol-2-yl)-4-(methylsulfonyl)benzamide
- 25 143. 5-(aminosulfonyl)-2,4-dichloro-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide
144. 5-(aminosulfonyl)-4-chloro-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide
145. 3-fluoro-N-(5-isopropyl-1,3-thiazol-2-yl)-4-methoxybenzamide
- 30 146. 3-chloro-N-(5-isopropyl-1,3-thiazol-2-yl)-4-methoxybenzamide
147. 5-chloro-N-(5-isopropyl-1,3-thiazol-2-yl)-2-methoxybenzamide
148. N-(5-isopropyl-1,3-thiazol-2-yl)-4-methoxybenzamide
- 35 149. N-(5-isopropyl-1,3-thiazol-2-yl)-3-methoxybenzamide
150. N-(5-isopropyl-1,3-thiazol-2-yl)-2-methoxybenzamide
151. N-(5-isopropyl-1,3-thiazol-2-yl)-3,4-dimethoxybenzamide

152. N-(5-isopropyl-1,3-thiazol-2-yl)-3,5-dimethoxybenzamide
153. N-(5-isopropyl-1,3-thiazol-2-yl)-2,4-dimethoxybenzamide
- 5 154. N-(5-isopropyl-1,3-thiazol-2-yl)-2,3-dimethoxybenzamide
155. N-(5-isopropyl-1,3-thiazol-2-yl)-3-phenoxybenzamide
156. N-(5-isopropyl-1,3-thiazol-2-yl)-2-phenoxybenzamide
157. N-(5-isopropyl-1,3-thiazol-2-yl)-4-phenoxybenzamide
- 10 158. 2-ethoxy-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide
159. 4-ethoxy-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide
160. N-(5-isopropyl-1,3-thiazol-2-yl)-3,4,5-trimethoxybenzamide
161. 3,4-diethoxy-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide
- 15 162. 3,4,5-triethoxy-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide
163. N-(5-isopropyl-1,3-thiazol-2-yl)-3-methoxy-4-(methoxymethoxy)benzamide
164. 4-butoxy-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide
- 20 165. N-(5-isopropyl-1,3-thiazol-2-yl)-4-propoxybenzamide
166. 4-isopropoxy-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide
167. N-(5-isopropyl-1,3-thiazol-2-yl)-1,3-benzodioxole-5-carboxamide
168. 4-(benzyloxy)-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide
- 25 169. 4-(2-cyclohexen-1-yloxy)-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide
170. N-(5-isopropyl-1,3-thiazol-2-yl)-4-(trifluoromethoxy)benzamide
- 30 171. 4-(difluoromethoxy)-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide
172. N-(5-isopropyl-1,3-thiazol-2-yl)-4-(methylsulfanyl)benzamide
173. 2-[(4-chlorophenyl)sulfinyl]-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide
- 35 174. N-(5-isopropyl-1,3-thiazol-2-yl)-2-[(4-nitrophenyl)sulfinyl]benzamide

175. N-(5-isopropyl-1,3-thiazol-2-yl)-4-[(4-methylphenyl)sulfonyl]-3-nitrobenzamide

176. N-(5-isopropyl-1,3-thiazol-2-yl)-3-[(trifluoromethyl)sulfanyl]benzamide

5 177. N-(5-isopropyl-1,3-thiazol-2-yl)-2-methoxy-4-(methylsulfanyl)benzamide

178. 2-[(2-cyanophenyl)sulfanyl]-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide

179. N~1~,N~1~-diethyl-3,6-difluoro-N~2~- (5-isopropyl-1,3-thiazol-2-yl)phthalamide

10 180. 4-formyl-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide

181. 2-formyl-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide

182. 4-{{(2,5-dimethoxyanilino)carbonyl}amino}-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide

15 183. 4-(hydroxymethyl)-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide

184. 4-{{(5-isopropyl-1,3-thiazol-2-yl)amino}carbonyl}-2-nitrobenzyl acetate

185. 4-{{(5-isopropyl-1,3-thiazol-2-yl)amino}carbonyl}-2-nitrobenzyl 4-(acetylamino)-3-iodobenzoate

20 186. 4-(acetylamino)-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide

187. N-(5-isopropyl-1,3-thiazol-2-yl)-4-[(2-phenylacetyl)amino]benzamide

25 188. 4-(acetylamino)-3-iodo-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide

189. 4-amino-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide

190. 4-(dimethylamino)-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide

30 191. 3-(dimethylamino)-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide

192. 2-(methylamino)-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide

193. N-(5-isopropyl-1,3-thiazol-2-yl)-2-[3-(trifluoromethyl)anilino]benzamide

35 194. 3-{{(5-bromo-1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl)methyl}amino}-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide

195. N-(5-isopropyl-1,3-thiazol-2-yl)-4-(1H-pyrrol-1-yl)benzamide
196. 2,6-dichloro-N-(5-isopropyl-1,3-thiazol-2-yl)isonicotinamide
- 5 197. 2-(4-bromophenyl)-6-(4-iodophenyl)-N-(5-isopropyl-1,3-thiazol-2-yl)isonicotinamide
198. N-(5-isopropyl-1,3-thiazol-2-yl)-2-[3-(trifluoromethyl)anilino]nicotinamide
199. 2,6-dichloro-N-(5-isopropyl-1,3-thiazol-2-yl)nicotinamide
- 10 200. 5,6-dichloro-N-(5-isopropyl-1,3-thiazol-2-yl)nicotinamide
201. 2-chloro-N-(5-isopropyl-1,3-thiazol-2-yl)-6-methylnicotinamide
- 15 202. 2,6-dichloro-5-fluoro-N-(5-isopropyl-1,3-thiazol-2-yl)nicotinamide
203. N-(5-isopropyl-1,3-thiazol-2-yl)-2-phenoxylicotinamide
204. N-(5-isopropyl-1,3-thiazol-2-yl)-6-(2,2,2-trifluoroethoxy)nicotinamide
205. N-(5-isopropyl-1,3-thiazol-2-yl)-2,6-dimethoxynicotinamide
- 20 206. N-(5-isopropyl-1,3-thiazol-2-yl)-2-quinoxalinecarboxamide
207. N-(5-isopropyl-1,3-thiazol-2-yl)-5-methyl-2-pyrazinecarboxamide
- 25 208. N-(5-isopropyl-1,3-thiazol-2-yl)-8-quinolinecarboxamide
209. N-(5-isopropyl-1,3-thiazol-2-yl)-2-phenyl-4-quinolinecarboxamide
- 30 210. N-(5-isopropyl-1,3-thiazol-2-yl)-5-methyl-1-phenyl-1H-pyrazole-4-carboxamide
211. N-(5-isopropyl-1,3-thiazol-2-yl)-5-methyl-1H-pyrazole-3-carboxamide
212. N-(5-isopropyl-1,3-thiazol-2-yl)-1H-pyrazole-4-carboxamide
- 35 213. N-(5-isopropyl-1,3-thiazol-2-yl)-5-methyl-2-phenyl-2H-1,2,3-triazole-4-carboxamide

WO 00/26202

-96-

214. 2-[(2,1,3-benzoxadiazol-5-yloxy)methyl]-N-(5-isopropyl-1,3-thiazol-2-yl)-4-methyl-1,3-thiazole-5-carboxamide

215. N-(5-isopropyl-1,3-thiazol-2-yl)-7-methoxy-1-carboxamide

216. N-(5-isopropyl-1,3-thiazol-2-yl)-9H-fluorene-1-benzofuran-2-carboxamide

217. N-(5-isopropyl-1,3-thiazol-2-yl)-1-[(4-methylphenyl)sulfonyl]-1H-pyrrole-3-carboxamide

218. 2-ethoxy-N-(5-isopropyl-1,3-thiazol-2-yl)-1-naphthamide

219. 4-fluoro-N-(5-isopropyl-1,3-thiazol-2-yl)-2-naphthamide

220. N-(5-isopropyl-1,3-thiazol-2-yl)-9,10-dioxo-9,10-naphthamide

221. N-(5-isopropyl-1,3-thiazol-2-yl)-1-dihydro-2-anthracenecarboxamide

222. N-(5-isopropyl-1,3-thiazol-2-yl)-9-oxo-9H-fluorene-4-carboxamide

223. N-(5-isopropyl-1,3-thiazol-2-yl)-9-oxo-9H-fluorene-1-carboxamide

224. N-(5-isopropyl-1,3-thiazol-2-yl)-8-oxo-5,6,7,8-tetrahydro-2-naphthalenecarboxamide

225. N-(5-isopropyl-1,3-thiazol-2-yl)-1,3-dioxo-1,3-dihydro-2-benzofuran-5-carboxamide

226. N-(5-isopropyl-1,3-thiazol-2-yl)-1H-indole-4-carboxamide

227. N-(5-isopropyl-1,3-thiazol-2-yl)-1H-indole-4-carboxamide

228. N-(5-isopropyl-1,3-thiazol-2-yl)-1-methyl-2-phenyl-1H-indole-5-carboxamide

229. 2-butyl-N-(5-isopropyl-1,3-thiazol-2-yl)-1H-indole-4-indole-5-carboxamide

230. N-(5-isopropyl-1,3-thiazol-2-yl)-1-methyl-2-phenyl-1H-carboxamide

231. N-(5-isopropyl-1,3-thiazol-2-yl)-1H-indole-6-2-carboxamide

232. 1-allyl-2-butyl-N-(5-isopropyl-1,3-thiazol-2-yl)-1H-indole-5-carboxamide

233. N-(5-isopropyl-1,3-thiazol-2-yl)-1-methyl-1H-indole-2-carboxamide

234. 1-benzyl-N-(5-isopropyl-1,3-thiazol-2-yl)-2-phenyl-1H-indole-5-carboxamide

5 235. N-(5-isopropyl-1,3-thiazol-2-yl)-1H-1,2,3-benzotriazole-5-carboxamide

236. N-(5-isopropyl-1,3-thiazol-2-yl)-3,5-dimethyl-4-isoxazolecarboxamide

237. N-(5-isopropyl-1,3-thiazol-2-yl)-3-thiophenecarboxamide

10 238. N-(5-isopropyl-1,3-thiazol-2-yl)-3-methyl-2-thiophenecarboxamide

239. N-(5-isopropyl-1,3-thiazol-2-yl)-5-methyl-2-thiophenecarboxamide

15 240. 5-bromo-N-(5-isopropyl-1,3-thiazol-2-yl)-2-thiophenecarboxamide

241. N-(5-isopropyl-1,3-thiazol-2-yl)-3-[(2,3,3-trichloroacryloyl)amino]-2-thiophenecarboxamide

242. 5-bromo-N-(5-isopropyl-1,3-thiazol-2-yl)-2-furamide

20 243. N-(5-isopropyl-1,3-thiazol-2-yl)-2-furamide

244. N-(5-isopropyl-1,3-thiazol-2-yl)-5-(4-nitrophenyl)-2-furamide

245. N-(5-isopropyl-1,3-thiazol-2-yl)-5-(2-nitrophenyl)-2-furamide

25 246. 5-(4-chlorophenyl)-N-(5-isopropyl-1,3-thiazol-2-yl)-2-furamide

247. N-(5-isopropyl-1,3-thiazol-2-yl)-5-[3-(trifluoromethyl)phenyl]-2-furamide

248. 5-(4-chloro-2-nitrophenyl)-N-(5-isopropyl-1,3-thiazol-2-yl)-2-furamide

30 249. N-(5-isopropyl-1,3-thiazol-2-yl)-5-(4-methyl-2-nitrophenyl)-2-furamide

250. 5-[2-chloro-5-(trifluoromethyl)phenyl]-N-(5-isopropyl-1,3-thiazol-2-yl)-2-furamide

35 251. tert-butyl (1R)-2-[(5-isopropyl-1,3-thiazol-2-yl)amino]-2-oxo-1-phenylethylcarbamate

252. (1R)-2-[(5-isopropyl-1,3-thiazol-2-yl)amino]-2-oxo-1-phenylethyl acetate

253. (1S)-2-[(5-isopropyl-1,3-thiazol-2-yl)amino]-2-oxo-1-phenylethyl acetate

254. (R,S)-2-fluoro-N-(5-isopropyl-1,3-thiazol-2-yl)-2-phenylacetamide

5 255. (R)-2-fluoro-N-(5-isopropyl-1,3-thiazol-2-yl)-2-phenylacetamide

256. (S)-2-fluoro-N-(5-isopropyl-1,3-thiazol-2-yl)-2-phenylacetamide

257. 2-(acetylamino)-N-(5-isopropyl-1,3-thiazol-2-yl)-2-phenylacetamide

10 258. (R,S)-2-(methoxy)-N-(5-isopropyl-1,3-thiazol-2-yl)-2-phenylacetamide

259. (R)-2-(methoxy)-N-(5-isopropyl-1,3-thiazol-2-yl)-2-phenylacetamide

15 260. (S)-2-(methoxy)-N-(5-isopropyl-1,3-thiazol-2-yl)-2-phenylacetamide

261. 3,3,3-trifluoro-N-(5-isopropyl-1,3-thiazol-2-yl)-2-methoxy-2-phenylpropanamide

262. N-(5-isopropyl-1,3-thiazol-2-yl)-2-(1-naphthyl)acetamide

20 263. N-(5-isopropyl-1,3-thiazol-2-yl)-2-(2-naphthyl)acetamide

264. 2-(1H-indol-3-yl)-N-(5-isopropyl-1,3-thiazol-2-yl)acetamide

25 265. 2-(1,3-benzodioxol-4-yl)-N-(5-isopropyl-1,3-thiazol-2-yl)acetamide

266. 2-(2,4-dinitrophenyl)-N-(5-isopropyl-1,3-thiazol-2-yl)acetamide

267. N-(5-isopropyl-1,3-thiazol-2-yl)-2-(2-methyl-1H-indol-3-yl)acetamide

30 268. N-(5-isopropyl-1,3-thiazol-2-yl)-2-(1-methyl-1H-indol-3-yl)acetamide

269. N-(5-isopropyl-1,3-thiazol-2-yl)-2-(5-methoxy-1H-indol-3-yl)acetamide

35 270. N-(5-isopropyl-1,3-thiazol-2-yl)-2-(5-benzyloxy-1H-indol-3-yl)acetamide

271. N-(5-isopropyl-1,3-thiazol-2-yl)-2-(3-methoxy-2-methyl-1H-indol-3-yl)acetamide

272. 2-(1H-indol-3-yl)-N-(5-isopropyl-1,3-thiazol-2-yl)-2-oxoacetamide

273. 2-(5-bromo-1H-indol-3-yl)-N-(5-isopropyl-1,3-thiazol-2-yl)acetamide

5 274. 2-(5-fluoro-1H-indol-3-yl)-N-(5-isopropyl-1,3-thiazol-2-yl)acetamide

275. 2-[1-(4-chlorobenzoyl)-5-methoxy-2-methyl-1H-indol-3-yl]-N-(5-isopropyl-1,3-thiazol-2-yl)acetamide

10 276. 3-(1H-indol-3-yl)-N-(5-isopropyl-1,3-thiazol-2-yl)propanamide

277. 4-(1H-indol-3-yl)-N-(5-isopropyl-1,3-thiazol-2-yl)butanamide

278. N-(5-isopropyl-1,3-thiazol-2-yl)-3-(2-thienyl)propanamide

15 279. N-(5-isopropyl-1,3-thiazol-2-yl)-2-(2-thienyl)acetamide

280. N-(5-isopropyl-1,3-thiazol-2-yl)-2-oxo-2-(2-thienyl)acetamide

281. N-(5-isopropyl-1,3-thiazol-2-yl)-2-(3-thienyl)acetamide

20 282. 2-(5-chloro-1-benzothiophen-3-yl)-N-(5-isopropyl-1,3-thiazol-2-yl)acetamide

283. 2-(1-benzothiophen-3-yl)-N-(5-isopropyl-1,3-thiazol-2-yl)acetamide

25 284. 2-[2-(formylamino)-1,3-thiazol-4-yl]-N-(5-isopropyl-1,3-thiazol-2-yl)-2-(methoxyimino)acetamide

285. 2-{2-[(2-chloroacetyl)amino]-1,3-thiazol-4-yl}-N-(5-isopropyl-1,3-thiazol-2-yl)-2-(methoxyimino)acetamide

286. 2-chloro-N-(4-{2-[(5-isopropyl-1,3-thiazol-2-yl)amino]-2-oxoethyl}-1,3-thiazol-2-yl)acetamide

30 287. ethyl 2-({2-[(5-isopropyl-1,3-thiazol-2-yl)amino]-2-oxo-1-(1H-pyrazol-3-yl)ethylidene}amino)oxy)acetate

288. 2-(2-furyl)-N-(5-isopropyl-1,3-thiazol-2-yl)-2-oxoacetamide

35 289. 2-(5-bromo-3-pyridinyl)-N-(5-isopropyl-1,3-thiazol-2-yl)acetamide

290. N-(5-isopropyl-1,3-thiazol-2-yl)-2-(7-methoxy-2-oxo-2H-chromen-4-yl)acetamide

291. N-(5-isopropyl-1,3-thiazol-2-yl)-4-phenyl-3-butenamide
292. N-(5-isopropyl-1,3-thiazol-2-yl)-4-oxo-4-(4-methyl-phenyl)butanamide
293. N-(5-isopropyl-1,3-thiazol-2-yl)-4-(4-nitrophenyl)butanamide
294. N-(5-isopropyl-1,3-thiazol-2-yl)-4-phenylbutanamide
295. benzyl 4-[(5-isopropyl-1,3-thiazol-2-yl)amino]-4-oxobutylcarbamate
296. methyl 5-[(5-isopropyl-1,3-thiazol-2-yl)amino]-5-oxopentanoate
297. 4-(1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl)-N-(5-isopropyl-1,3-thiazol-2-yl)butanamide
298. N-(5-isopropyl-1,3-thiazol-2-yl)-4-(4-methoxy-1-naphthyl)-4-oxobutanamide
299. 3-(2-chlorophenoxy)-N-(5-isopropyl-1,3-thiazol-2-yl)propanamide
300. 3-(4-methylphenoxy)-N-(5-isopropyl-1,3-thiazol-2-yl)propanamide
301. 3-cyclopentyl-N-(5-isopropyl-1,3-thiazol-2-yl)propanamide
302. 3-cyclohexyl-N-(5-isopropyl-1,3-thiazol-2-yl)propanamide
303. N-(5-isopropyl-1,3-thiazol-2-yl)-4-methylpentanamide
304. 3-(4-chlorophenyl)-N-(5-isopropyl-1,3-thiazol-2-yl)propanamide
305. 3-(4-methoxyphenyl)-N-(5-isopropyl-1,3-thiazol-2-yl)propanamide
306. 3-chloro-N-(5-isopropyl-1,3-thiazol-2-yl)propanamide
307. 3-phenyl-N-(5-isopropyl-1,3-thiazol-2-yl)propanamide
308. 2-cyclohexyl-N-(5-isopropyl-1,3-thiazol-2-yl)acetamide
309. N-(5-isopropyl-1,3-thiazol-2-yl)-3-methylbutanamide
310. N-(5-isopropyl-1,3-thiazol-2-yl)-5-oxo-5-phenylpentanamide
311. 2-[(5-isopropyl-1,3-thiazol-2-yl)amino]-2-oxo-1-phenylethyl acetate
312. N-(5-isopropyl-1,3-thiazol-2-yl)-2-[4-(1-oxo-1,3-dihydro-2H-isoindol-2-yl)phenyl]propanamide

WO 00/26202

- 101 -

313. 1-(4-chlorophenyl)-N-(5-isopropyl-1,3-thiazol-2-yl)cyclopentanecarboxamide
314. 1-phenyl-N-(5-isopropyl-1,3-thiazol-2-yl)cyclopentanecarboxamide
5 315. 2-(3-bromo-4-methoxyphenyl)-N-(5-isopropyl-1,3-thiazol-2-yl)acetamide
316. 2-(2-nitro-4-trifluoromethylphenyl)-N-(5-isopropyl-1,3-thiazol-2-yl)acetamide
10 317. 5-cyclohexyl 1-(4-{2-[5-isopropyl-1,3-thiazol-2-yl]acetoxy}carbonyl)benzyl (2S)-2-[(tert-
yl)amino]-2-oxoethyl)pentanedioate
318. 2-(5,6-dimethyl-1H-benzimidazol-1-yl)-N-(5-isopropyl-1,3-thiazol-2-yl)acetamide
15 319. 2-[5-(4-chlorophenyl)-2H-1,2,3,4-tetraazol-2-yl]acetamide
320. N-(5-isopropyl-1,3-thiazol-2-yl)-2-[5-(1-pyrrolidinyl)-2H-1,2,3,4-tetraazol-2-yl]acetamide
321. N-(5-isopropyl-1,3-thiazol-2-yl)-2-(3-methyl-1-benzothiophen-2-yl)acetamide
20 322. N-(5-isopropyl-1,3-thiazol-2-yl)-4,4-bis(4-methylphenyl)-3-butenamide
323. 2-cyclopropyl-N-(5-isopropyl-1,3-thiazol-2-yl)acetamide
25 324. N-(4-bromo-6-[(5-isopropyl-1,3-thiazol-2-yl)amino]-6-oxohexyl)benzamide
325. 2-cyclopentyl-N-(5-isopropyl-1,3-thiazol-2-yl)acetamide
326. benzyl 6-[(5-isopropyl-1,3-thiazol-2-yl)amino]-6-oxohexylcarbamate
30 327. N-1-(5-isopropyl-1,3-thiazol-2-yl)-N-4-(2-propynyl)-2-butenediamide
328. 4-(2,4-dimethylphenyl)-N-(5-isopropyl-1,3-thiazol-2-yl)-N-4-(2-propynyl)-
35 329. 4-(4-benzylloxyphenyl)-N-(5-isopropyl-1,3-thiazol-2-yl)-N-4-(thiophen-2-yl)-4-oxobutanamide
330. 4-(thiophen-2-yl)-N-(5-isopropyl-1,3-thiazol-2-yl)-4-oxobutanamide

331. benzyl 2-[(benzyloxy)carbonyl]amino]-5-[(5-isopropyl-1,3-thiazol-2-yl)amino]-5-oxopentanoate

332. 4-(1H-indol-3-yl)-N-{3-[(5-isopropyl-1,3-thiazol-2-yl)amino]-3-oxopropyl}butanamide

5 333. 4-[(5-isopropyl-1,3-thiazol-2-yl)amino]carbonylphenyl 4-chlorobenzenesulfonate

334. N-(5-isopropyl-1,3-thiazol-2-yl)-4-[(2-methoxyanilino)carbonyl]amino}benzamide

335. 4-[(2-(isopropylsulfonyl)acetyl]amino)-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide

10 336. N-(5-isopropyl-1,3-thiazol-2-yl)-4-[(2-(phenylsulfanyl)acetyl]amino}benzamide

337. 4-[(diethylamino)sulfonyl]-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide

15 338. 2-bromo-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide

339. 3,5-difluoro-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide

340. 3-[(2-fluoroanilino)carbonyl]amino)-N-(5-isopropyl-1,3-thiazol-2-yl)benzamide

20 341. N-(5-isopropyl-1,3-thiazol-2-yl)-1-phenyl-5-propyl-1H-pyrazole-4-carboxamide

342. 3-chloro-4-(isopropylsulfonyl)-N-(5-isopropyl-1,3-thiazol-2-yl)-5-(methylsulfanyl)-2-thiophenecarboxamide

343. 3-iodo-4-(isopropylsulfonyl)-N-(5-isopropyl-1,3-thiazol-2-yl)-5-(methylsulfanyl)-2-thiophenecarboxamide

25 344. 2-[(4-chlorophenyl)sulfonylmethyl]-N-(5-isopropyl-1,3-thiazol-2-yl)-4-methyl-1,3-thiazole-5-carboxamide

345. 5-(4-chlorophenyl)-N-(5-isopropyl-1,3-thiazol-2-yl)-2-(trifluoromethyl)-3-furamide

30 346. N-(5-isopropyl-1,3-thiazol-2-yl)-2-(2,3,4,5,6-pentafluorophenyl)acetamide

347. N-(5-isopropyl-1,3-thiazol-2-yl)-2-(2-fluorophenyl)acetamide

35 348. N-(5-isopropyl-1,3-thiazol-2-yl)-2-(2-bromophenyl)acetamide

349. N-(5-isopropyl-1,3-thiazol-2-yl)-2-(2-chlorophenyl)acetamide

350. N-(5-isopropyl-1,3-thiazol-2-yl)-2-(2-nitrophenyl)acetamide
351. N-(5-isopropyl-1,3-thiazol-2-yl)-2-(2-trifluoromethylphenyl)acetamide
- 5 352. N-(5-isopropyl-1,3-thiazol-2-yl)-2-(2-methoxyphenyl)acetamide
353. N-(5-isopropyl-1,3-thiazol-2-yl)-2-(2,5-dimethoxyphenyl)acetamide
- 10 354. N-(5-isopropyl-1,3-thiazol-2-yl)-2-(2,5-difluorophenyl)acetamide
355. N-(5-isopropyl-1,3-thiazol-2-yl)-2-(3,4,5-trimethoxyphenyl)acetamide
356. N-(5-isopropyl-1,3-thiazol-2-yl)-2-(2,6-dichlorophenyl)acetamide
- 15 357. N-(5-isopropyl-1,3-thiazol-2-yl)-2-(2-chloro-6-fluorophenyl)acetamide
358. N-(5-isopropyl-1,3-thiazol-2-yl)-2-(3,5-dimethoxyphenyl)acetamide
359. N-(5-isopropyl-1,3-thiazol-2-yl)-2-(3,5-difluorophenyl)acetamide
- 20 360. N-(5-isopropyl-1,3-thiazol-2-yl)-2-(2,5-bis-trifluoromethylphenyl)acetamide
361. N-(5-isopropyl-1,3-thiazol-2-yl)-2-(4-methylthiophenyl)acetamide
- 25 362. N-(5-isopropyl-1,3-thiazol-2-yl)-2-(4-methoxyphenyl)acetamide
363. N-(5-isopropyl-1,3-thiazol-2-yl)-2-(4-bromophenyl)acetamide
364. N-(5-isopropyl-1,3-thiazol-2-yl)-2-(4-chlorophenyl)acetamide
- 30 365. N-(5-isopropyl-1,3-thiazol-2-yl)-2-(4-fluorophenyl)acetamide
366. N-(5-isopropyl-1,3-thiazol-2-yl)-2-(4-nitrophenyl)acetamide
- 35 367. N-(5-isopropyl-1,3-thiazol-2-yl)-2-(4-trifluoromethylphenyl)acetamide
368. N-(5-isopropyl-1,3-thiazol-2-yl)-2-(4-methylphenyl)acetamide

369. N-(5-isopropyl-1,3-thiazol-2-yl)-2-(4-dimethylaminophenyl)acetamide

370. 2-[1,1'-biphenyl]-4-yl-N-(5-isopropyl-1,3-thiazol-2-yl)acetamide

5 371. N-(5-isopropyl-1,3-thiazol-2-yl)-2-(3-trifluoromethylphenyl)acetamide

372. N-(5-isopropyl-1,3-thiazol-2-yl)-2-(3-bromophenyl)acetamide

10 373. N-(5-isopropyl-1,3-thiazol-2-yl)-2-(3-chlorophenyl)acetamide

374. N-(5-isopropyl-1,3-thiazol-2-yl)-2-(3-nitrophenyl)acetamide

375. N-(5-isopropyl-1,3-thiazol-2-yl)-2-(3-methoxyphenyl)acetamide

15 376. N-(5-isopropyl-1,3-thiazol-2-yl)-2-(2,4-dinitrophenyl)acetamide

377. N-(5-isopropyl-1,3-thiazol-2-yl)-2-(2,4-dichlorophenyl)acetamide

378. N-(5-isopropyl-1,3-thiazol-2-yl)-2-(2,4-difluorophenyl)acetamide

20 379. N-(5-isopropyl-1,3-thiazol-2-yl)-2-(4-benzyloxy-3-methoxyphenyl)acetamide

380. N-(5-isopropyl-1,3-thiazol-2-yl)-2-(3,4-dichlorophenyl)acetamide

25 381. N-(5-isopropyl-1,3-thiazol-2-yl)-2-(3,4-difluorophenyl)acetamide

382. N-(5-isopropyl-1,3-thiazol-2-yl)-2-(3,4-dimethoxyphenyl)acetamide

383. 2-(2,3-dihydro-1H-inden-5-yl)-N-(5-isopropyl-1,3-thiazol-2-yl)acetamide

30 384. N-(5-isopropyl-1,3-thiazol-2-yl)-1-phenylcyclopropanecarboxamide

385. 2-cyclopentyl-N-(5-isopropyl-1,3-thiazol-2-yl)-2-phenylacetamide

35 386. 2-cyclohexyl-N-(5-isopropyl-1,3-thiazol-2-yl)-2-phenylacetamide

387. N-(5-isopropyl-1,3-thiazol-2-yl)-2,2-diphenylacetamide

388. N-(5-isopropyl-1,3-thiazol-2-yl)-2-(2-nitrophenoxy)acetamide

389. N-(5-isopropyl-1,3-thiazol-2-yl)-2-(4-nitrophenyl)propanamide

5 390. N-(5-isopropyl-1,3-thiazol-2-yl)-2-phenylpropanamide

391. N-(5-isopropyl-1,3-thiazol-2-yl)-2-(4-isobutylphenyl)propanamide

392. N-(5-isopropyl-1,3-thiazol-2-yl)-2-oxo-2-phenylacetamide

10 393. N-(5-isopropyl-1,3-thiazol-2-yl)-3-methyl-2-phenylpentanamide

394. (E, Z)-N-(5-isopropyl-1,3-thiazol-2-yl)-2-phenyl-2-butenamide

395. N-(5-isopropyl-1,3-thiazol-2-yl)bicyclo[4.2.0]octa-1,3,5-triene-7-carboxamide

15 396. N-(5-isopropyl-1,3-thiazol-2-yl)-3-oxo-1-indanecarboxamide

397. N-(5-isopropyl-1,3-thiazol-2-yl)-2-phenylbutanamide

398. tert-butyl (1S)-2-[(5-isopropyl-1,3-thiazol-2-yl)amino]-1-methyl-2-oxoethylcarbamate

20 399. tert-butyl (1S,2S)-1-[(5-isopropyl-1,3-thiazol-2-yl)amino]carbonyl]-2-methylbutylcarbamate

400. tert-butyl 2-[(5-isopropyl-1,3-thiazol-2-yl)amino]-2-oxoethylcarbamate

25 401. tert-butyl (1S)-5-amino-1-[(5-isopropyl-1,3-thiazol-2-yl)amino]carbonylpentylcarbamate

402. tert-butyl 4-[(imino{[(4-methylphenyl)sulfonyl]amino}methyl)amino]-1-[(5-isopropyl-1,3-thiazol-2-yl)amino]carbonylbutylcarbamate

30 403. tert-butyl 1-[(5-isopropyl-1,3-thiazol-2-yl)amino]carbonyl]-3-(tritylamo)propylcarbamate

404. tert-butyl (1S)-1-(benzyloxymethyl)-2-[(5-isopropyl-1,3-thiazol-2-yl)amino]-2-oxoethylcarbamate

35 405. tert-butyl (1S)-1-benzyl-2-[(5-isopropyl-1,3-thiazol-2-yl)amino]-2-oxoethylcarbamate

406. tert-butyl (1R)-2-[(5-isopropyl-1,3-thiazol-2-yl)amino]-2-oxo-1-(benzylthiomethyl)ethylcarbamate

407. benzyl (3S)-3-[(tert-butoxycarbonyl)amino]-4-[(5-isopropyl-1,3-thiazol-2-yl)amino]-4-oxobutanoate

408. tert-butyl (2S)-2-[(5-isopropyl-1,3-thiazol-2-yl)amino]carbonyl)-1-pyrrolidinecarboxylate

5 409. tert-butyl (1S)-1-(1H-indol-3-ylmethyl)-2-[(5-isopropyl-1,3-thiazol-2-yl)amino]-2-oxoethylcarbamate

410. tert-butyl (1S)-1-[(5-isopropyl-1,3-thiazol-2-yl)amino]carbonyl)-3-(methylsulfanyl)propylcarbamate

411. tert-butyl (1S)-2-benzyloxy-1-[(5-isopropyl-1,3-thiazol-2-yl)amino]carbonyl)propylcarbamate

10 412. tert-butyl (1S)-1-(4-benzyloxybenzyl)-2-[(5-isopropyl-1,3-thiazol-2-yl)amino]-2-oxoethylcarbamate

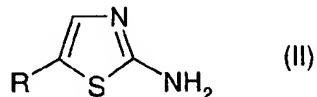
413. tert-butyl (1S)-1-[(5-isopropyl-1,3-thiazol-2-yl)amino]carbonyl)-2-methylpropylcarbamate

15 414. tert-butyl (1S)-1-[(5-isopropyl-1,3-thiazol-2-yl)amino]carbonyl)-3-methylbutylcarbamate

415. benzyl (4S)-4-[(tert-butoxycarbonyl)amino]-5-[(5-isopropyl-1,3-thiazol-2-yl)amino]-5-oxopentanoate
and the pharmaceutically acceptable salts thereof.

20

12. A process for producing a compound of formula (I), as defined in claim 7, which process comprises reacting a compound of formula (II)



25 with a compound of formula (III)



wherein R and R_1 are as defined in claim 7 and X is hydroxy or a suitable leaving group;
and, if desired, converting a 2-amino-1,3-thiazole derivative of formula (I) into another such derivative of formula (I), and/or into a salt thereof.

13. A process according to claim 12 wherein X is hydroxy, bromine or chlorine.

- 107 -

14. A pharmaceutical composition comprising one or more pharmaceutically acceptable carriers and/or diluents and, as the active principle, an effective amount of a compound of formula (I) as defined in claim 7.

INTERNATIONAL SEARCH REPORT

Int'l Application No
PCT/EP 99/08306A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C07D277/46 C07D417/12 A61K31/426 A61K31/427 A61P35/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 C07D A61K A61P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the International search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 98 04536 A (OTSUKA PHARMACEUTICAL COMPANY LIMITED) 5 February 1998 (1998-02-05) cited in the application page 101, line 22 -page 108, line 9; claims	1-14
X	EP 0 412 404 A (FUJISAWA PHARMACEUTICAL CO) 13 February 1991 (1991-02-13) cited in the application claims	1-14
X	US 4 027 031 A (DEBAUN JACK R ET AL) 31 May 1977 (1977-05-31) the whole document	1-14

 Further documents are listed in the continuation of box C. Patent family members are listed in annex.

* Special categories of cited documents :

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the International filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the International filing date but later than the priority date claimed

"T" later document published after the International filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the International search

Date of mailing of the International search report

16 February 2000

02/03/2000

Name and mailing address of the ISA
European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl
Fax (+31-70) 340-3016

Authorized officer

Henry, J

INTERNATIONAL SEARCH REPORT

Int. Appl. No.

PCT/EP 99/08306

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DE 21 28 941 A (SOCIETE MELLE-BEZONS) 16 December 1971 (1971-12-16) cited in the application claims ---	1-14
X	EP 0 261 503 A (VALEAS SPA) 30 March 1988 (1988-03-30) cited in the application claims ---	1-14
X	CHEMICAL ABSTRACTS, vol. 50, no. 1, 10 January 1956 (1956-01-10) Columbus, Ohio, US; abstract no. 964e, S.R.M.BUSHBY ET AL: "The antitrichomonal activity of amidonitrothiazoles" page 964; XP002130674 abstract & J.PHARM. AND PHARMACOL., vol. 7, 1955, pages 112-117, ---	1-14
X	CHEMICAL ABSTRACTS, vol. 61, no. 3, 3 August 1964 (1964-08-03) Columbus, Ohio, US; abstract no. 3087, MAX ROBBA ET AL: "Synthesis of thiazoles and isothiazoles. Their action on Trichomonas vaginalis and Candida albicans" XP002130675 abstract & ANN. PHARM. FRANC., vol. 22, no. 3, 1964, pages 201-210, ---	1-14
X	PETER J. ISLIP ET AL: "Schistosomicidal 5-nitro-4-thiazolines" JOURNAL OF MEDICINAL CHEMISTRY., vol. 15, no. 9, 1972, pages 951-954, XP002130668 AMERICAN CHEMICAL SOCIETY. WASHINGTON., US ISSN: 0022-2623 the whole document ---	1-14
X	ROGER D. WESTLAND ET AL: "Novel schistomocides. S-2-{2-2(2-thiazolylcarbamoyl)ethyl}amino ethyl hydrogen thiosulfate and related compounds" JOURNAL OF MEDICINAL CHEMISTRY., vol. 14, no. 10, 1971, pages 916-920, XP002130669 AMERICAN CHEMICAL SOCIETY. WASHINGTON., US ISSN: 0022-2623 the whole document ---	1-14
	-/-	

INTERNATIONAL SEARCH REPORT

Interinal Application No
PCT/EP 99/08306

C(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	LEIF GREHN: "A method for nitration of thiiazoles" JOURNAL OF HETEROCYCLIC CHEMISTRY., vol. 14, no. 5, August 1977 (1977-08), pages 917-919, XP002130670 HETERO CORPORATION. PROVO., US ISSN: 0022-152X the whole document ---	6-13
X	US 3 427 318 A (BARBER MICHAEL STUART ET AL) 11 February 1969 (1969-02-11) the whole document ---	6-13
X	H.ERLENMEYER ET AL: "Zur Kenntnis der Thiazol-4-sulfonsäure und der Thiazol-5-sulfonsäure" HELVETICA CHIMICA ACTA., vol. 28, 1945, pages 985-991, XP002130671 VERLAG HELVETICA CHIMICA ACTA. BASEL., CH ISSN: 0018-019X page 989 ---	6-13
X	FR 1 499 557 A (MAY AND BAKER LIMITED) 18 September 1967 (1967-09-18) claims ---	6-13
X	US 3 591 600 A (FANCHER LLEWELLYN W) 6 July 1971 (1971-07-06) the whole document ---	6-13
X	FR 1 488 625 A (TOYO KOATSU INDUSTRIES INC.) 5 June 1967 (1967-06-05) claims ---	6-13
X	DE 16 42 352 A (MITSUI TOATSU CHEMICALS) 24 February 1972 (1972-02-24) the whole document ---	6-13
X	CHARLES D. HURD ET AL: "The 2-aminothiazoles" JOURNAL OF THE AMERICAN CHEMICAL SOCIETY., vol. 71, December 1949 (1949-12), pages 4007-4010, XP002130672 AMERICAN CHEMICAL SOCIETY, WASHINGTON, DC., US ISSN: 0002-7863 the whole document ---	6-13
		-/-

INTERNATIONAL SEARCH REPORT

International Application No

PCT/EP 99/08306

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>TIMOTHY N. BIRKINSHAW ET AL: "Tautomerism in 2-trichloro- and 2-trifluoro-acetamidothiazoles" JOURNAL OF THE CHEMICAL SOCIETY, PERKIN TRANSACTIONS 1., 1982, pages 939-943, XP002130673 CHEMICAL SOCIETY, LETCHWORTH., GB ISSN: 0300-922X the whole document</p> <p>---</p>	6-13
X	<p>US 3 374 082 A (LEMIN ALAN J) 19 March 1968 (1968-03-19) the whole document</p> <p>---</p>	6-13
X	<p>CHEMICAL ABSTRACTS, vol. 81, no. 5, 5 August 1974 (1974-08-05) Columbus, Ohio, US; abstract no. 22258q, page 156; XP002130676 abstract</p>	6-13
X	<p>& JP 48 027467 B (SANKYO CO LTD) 22 August 1973 (1973-08-22) cited in the application</p> <p>---</p>	6-13
E	<p>WO 99 65884 A (BRISTOL- MYERS SQUIBB COMPANY) 23 December 1999 (1999-12-23) claims</p> <p>---</p>	1-14

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/EP 99/08306

Patent document cited in search report		Publication date	Patent family member(s)		Publication date
WO 9804536	A	05-02-1998	AU	695817 B 3635497 A CA 2233611 A CN 1198160 A EP 0858452 A JP 10095777 A	20-08-1998 20-02-1998 05-02-1998 04-11-1998 19-08-1998 14-04-1998
EP 0412404	A	13-02-1991	AT	133667 T 635758 B AU 6004590 A CA 2022731 A CN 1049337 A, B DE 69025104 D DE 69025104, T DK 412404 T ES 2082805 T FI 96857 B GR 3019009 T HK 151596 A HU 57752 A HU 9500375 A IL 95281 A JP 3068567 A NO 179638 B PH 26766 A PT 94925 A, B RU 2010026 C RU 2048468 C US 5369107 A US 5256675 A ZA 9005858 A	15-02-1996 01-04-1993 07-02-1991 08-02-1991 20-02-1991 14-03-1996 04-07-1996 26-02-1996 01-04-1996 31-05-1996 31-05-1996 16-08-1996 30-12-1991 28-09-1995 18-06-1996 25-03-1991 12-08-1996 28-09-1992 18-04-1991 30-03-1994 20-11-1995 29-11-1994 26-10-1993 29-05-1991
US 4027031	A	31-05-1977	AT	350316 B 98477 A AU 2220177 A BE 852075 A CA 1068607 A CH 626079 A DE 2708327 A FR 2348206 A GR 66154 A JP 52125164 A NL 7702432 A PH 11483 A PT 66258 A, B	25-05-1979 15-10-1978 17-08-1978 05-09-1977 24-12-1979 30-10-1981 03-11-1977 10-11-1977 19-01-1981 20-10-1977 18-10-1977 01-02-1978 01-04-1977
DE 2128941	A	16-12-1971	FR	2092714 A ES 392093 A ES 392094 A GB 1355718 A JP 50004664 B	28-01-1972 01-10-1974 01-08-1974 05-06-1974 22-02-1975
EP 0261503	A	30-03-1988	IT	1197259 B AT 74915 T DE 3778268 A	30-11-1988 15-05-1992 21-05-1992
US 3427318	A	11-02-1969	BE	677595 A CH 452994 A	09-09-1966

INTERNATIONAL SEARCH REPORT

Information on patent family members

Int'l. Application No

PCT/EP 99/08306

Patent document cited in search report	Publication date	Patent family member(s)		Publication date
US 3427318 A		DE 1542970 A		24-07-1969
		FR 1470974 A		03-05-1967
		GB 1145822 A		
		NL 6603112 A		12-09-1966
FR 1499557 A		OA 2283 A		05-05-1970
US 3591600 A	06-07-1971	ES 381519 A		16-01-1973
		US 3749775 A		31-07-1973
FR 1488625 A	02-11-1967	NONE		
DE 1642352 A	24-02-1972	NONE		
US 3374082 A	19-03-1968	GB 1124270 A		
JP 48027467 B	22-08-1973	NONE		
WO 9965884 A	23-12-1999	NONE		